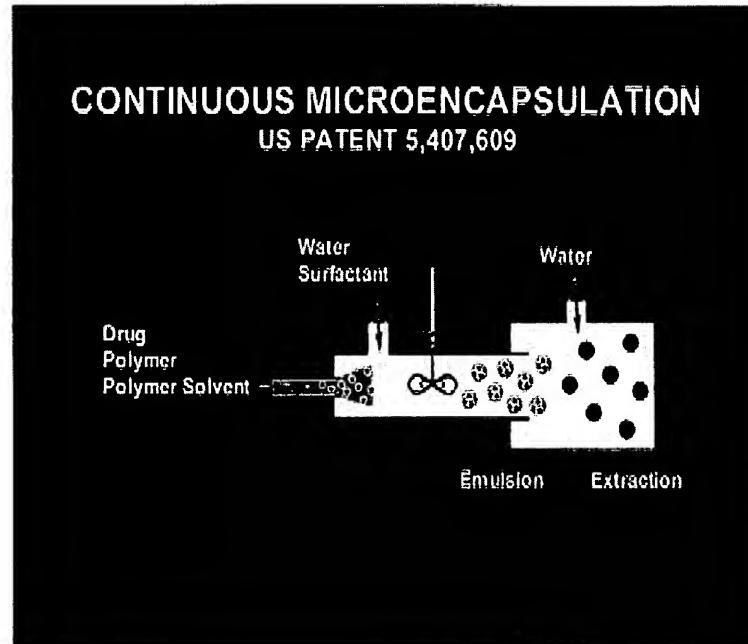




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### Advantages

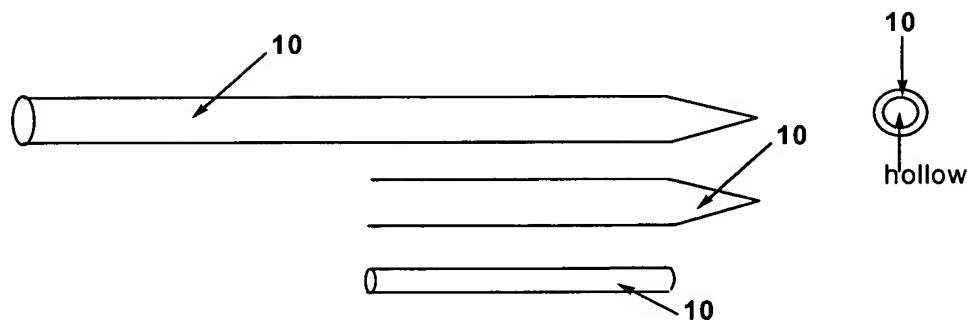
- US Patent issued 1995
- Fast encapsulation time -- milliseconds
- Minimal exposure to polymer solvent
- High encapsulation efficiency
- Good Yields
- Makes small microparticles  
<100 micron <10 micron

### Drugs Microencapsulated

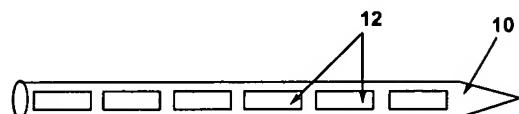
- Proteins
- Peptides
- Small molecules
- Water-soluble drugs
- Hydrophobic drugs
- Drugs encapsulated in lactide/glycolide polymers

Figure 1

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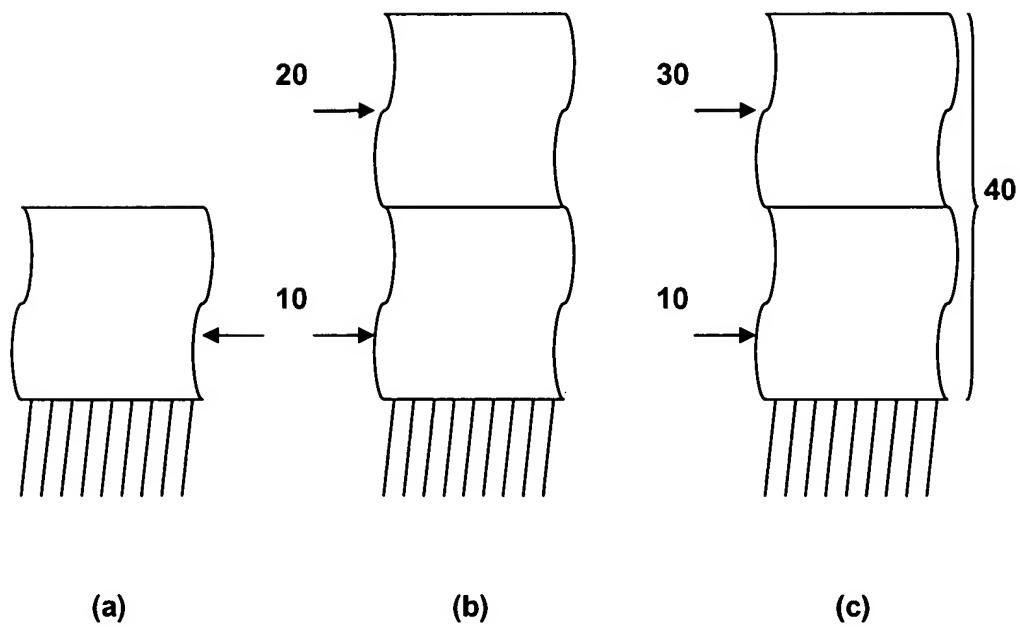


**Figure 2**



**Figure 3**

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**Figure 4**

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Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	3B	4B	F

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	9B	<9B	F

Hardness Rating: 2H-H-F-HB-B-2B-3B-4B-5B-6B-7B-8B-9B

Harder  Softer

**Figure 5**

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Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	<3mm

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	< 3mm

**Figure 6**

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Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Class:	5B	5B	5B	4B	5B

Class Rating: 5B = 0% of coating removed from substrate  
4B = Less than 5% of coating removed from substrate

**Figure 7**

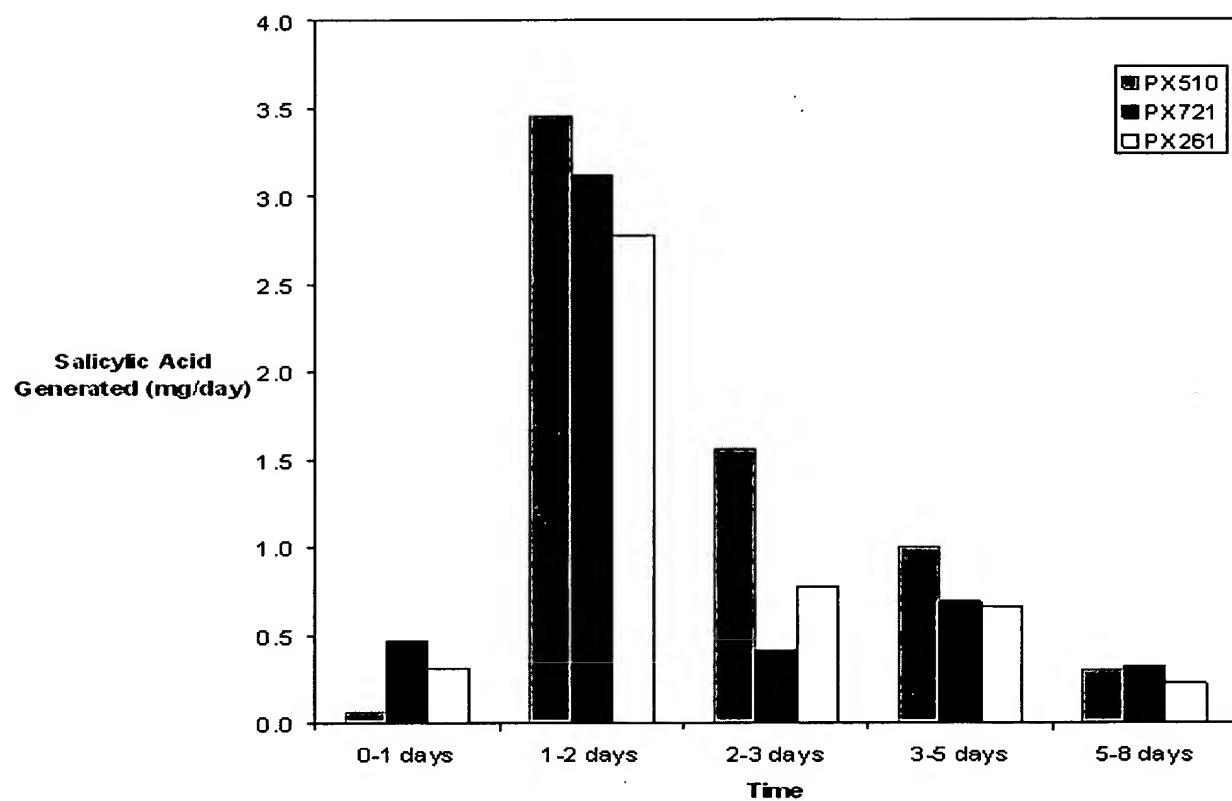
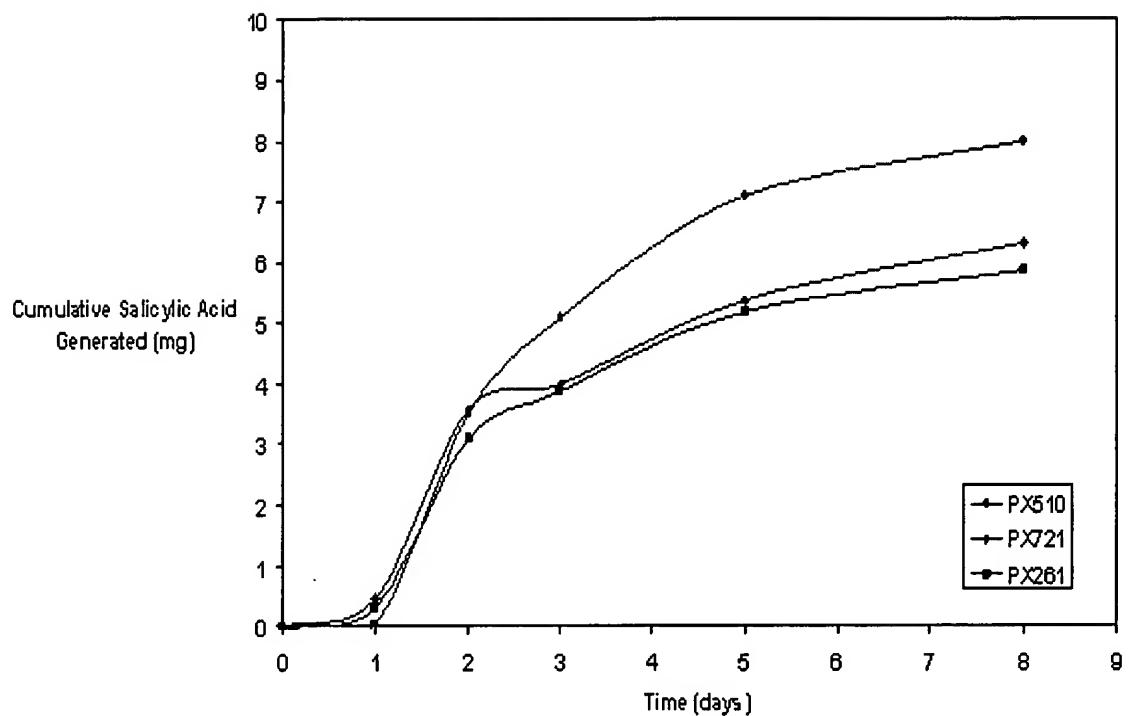
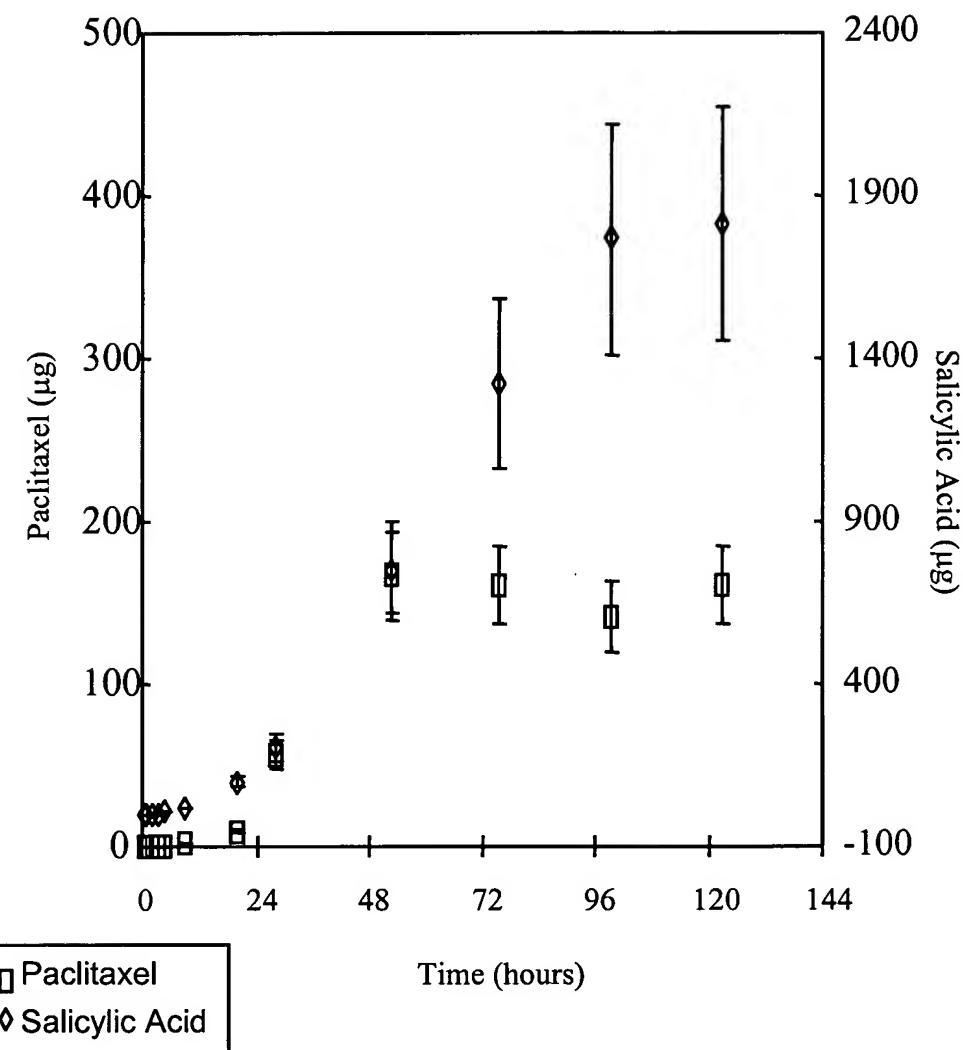


Figure 8A



**Figure 8B**



**Figure 9A**

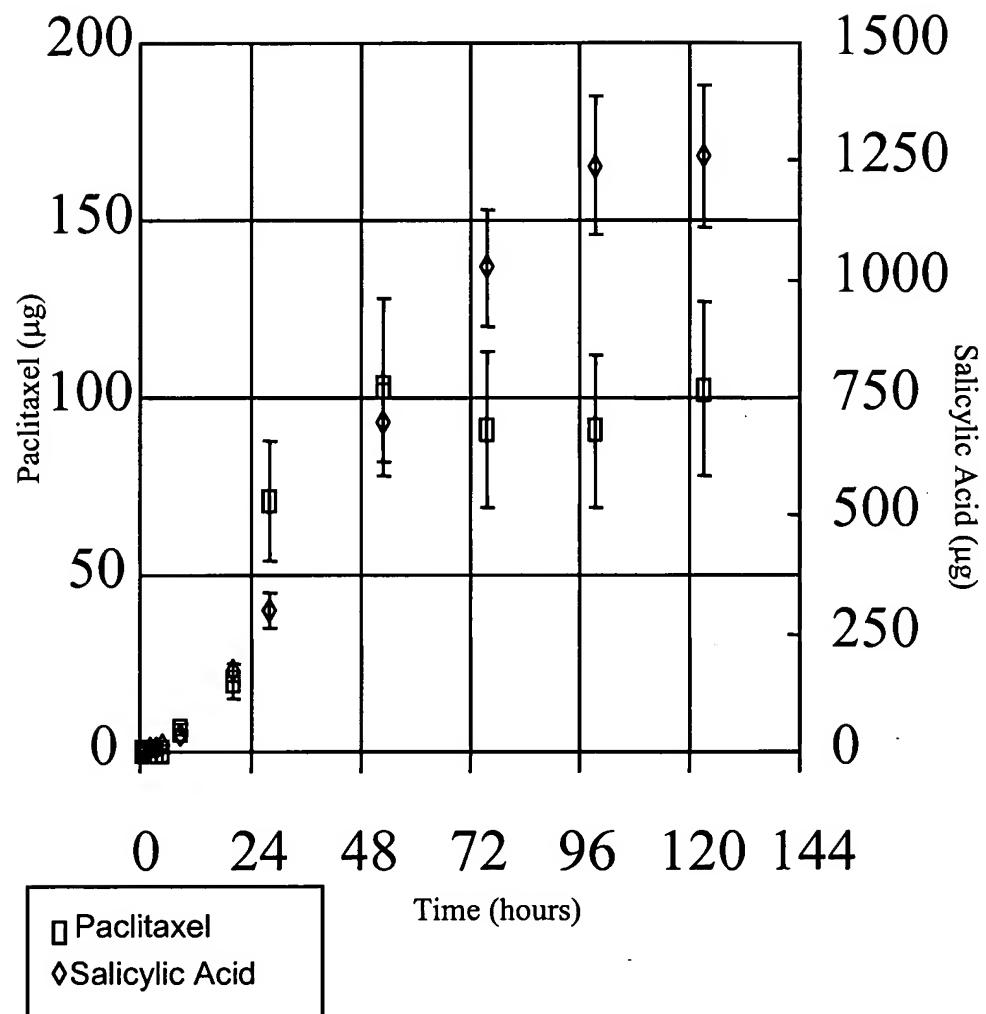
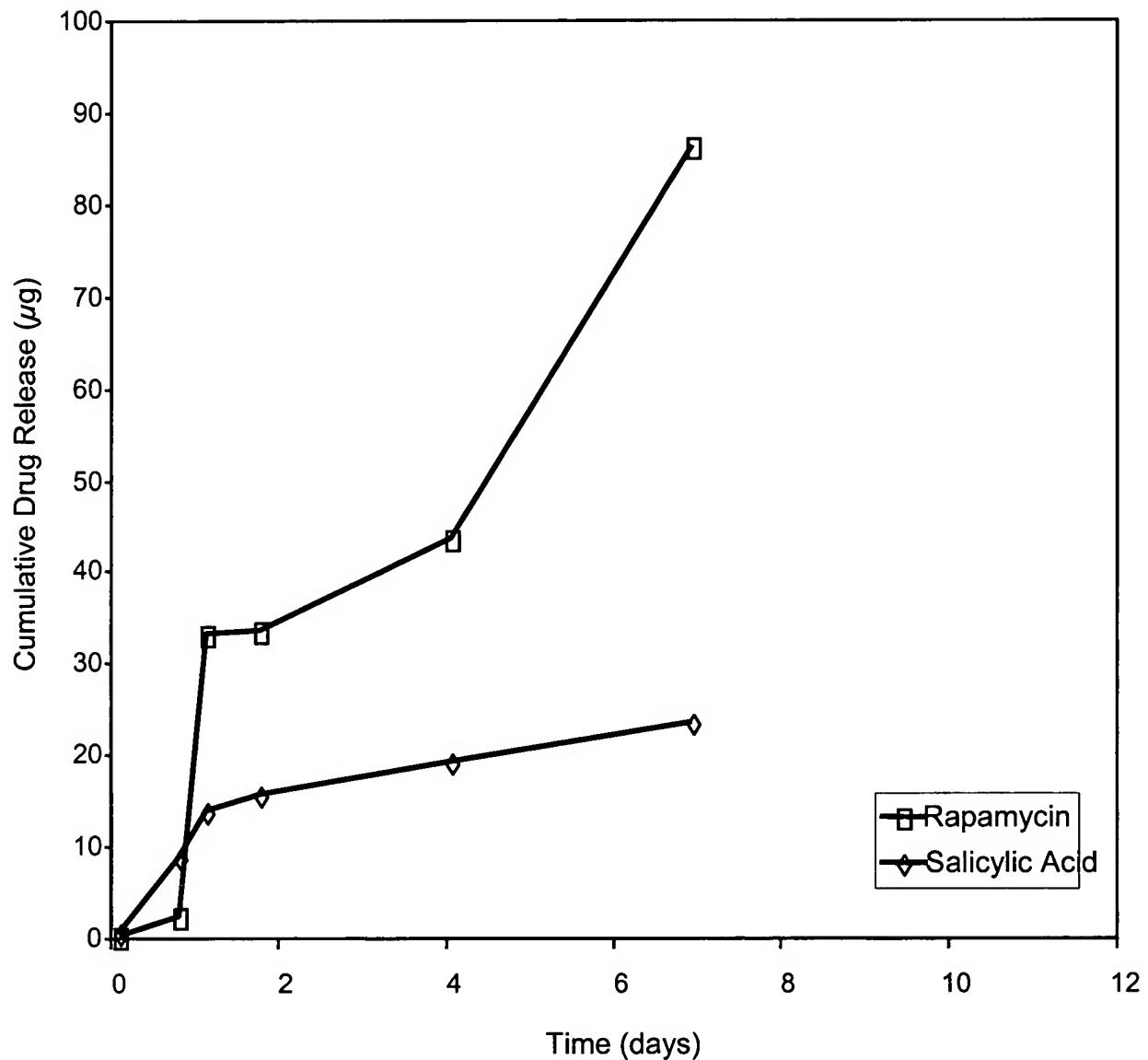


Figure 9B

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Property	Formulation			
	PX510	PX721	PX261	PX749
T <sub>g</sub> (°C)	44	38	29	16
Tensile modulus (MPa)	2.0 (25 °C) 5.1 (37 °C)			3.0 (25 °C)
Yield Strength (MPa)	Not observed			6.0 (25 °C)
Ultimate Elongation (%)	1.5 (25 °C) 350 (37 °C)			500 (25 °C)

**Figure 10**



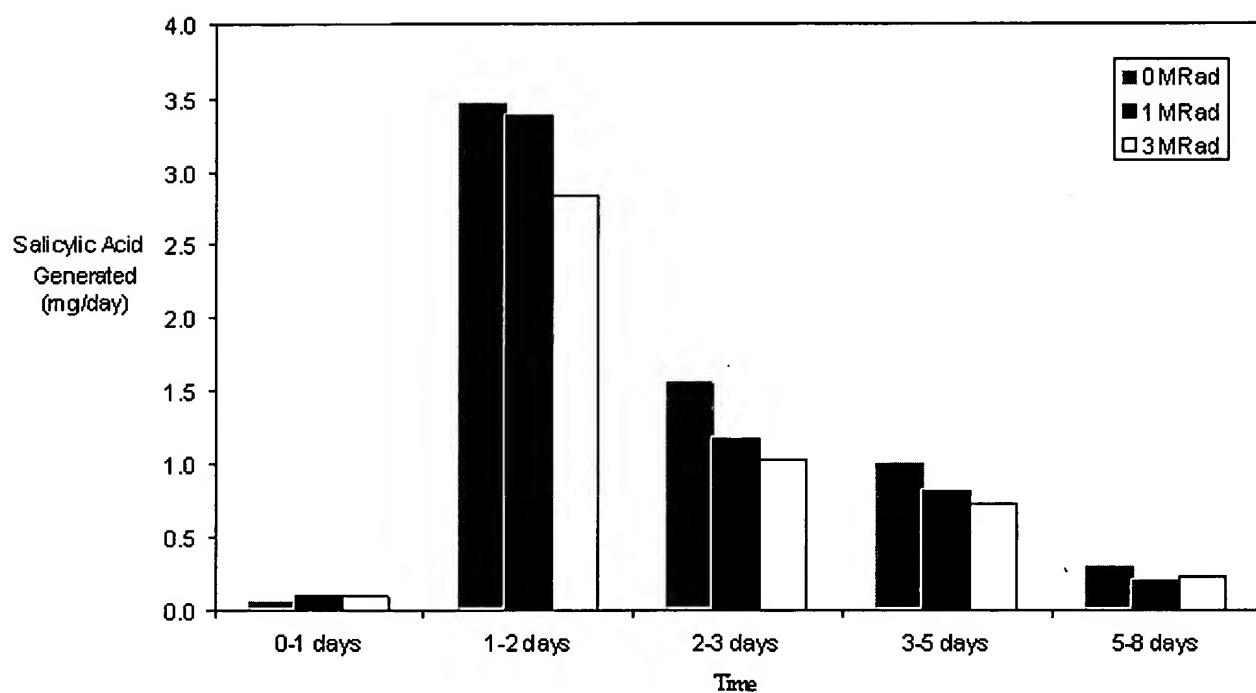
**Figure 11**

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Property	E Beam (3 MRad)			$\gamma$ (25-35 KGys)		
	PX510	PX721	PX261	PX510	PX721	PX261
MW	-26%	-39%	-26%	-14%	N/C	N/C
Hardness	-2 units	N/C	-1 unit	N/C	-3 units	-2 units
Flexibility	N/C	N/C	N/C	N/C	N/C	N/C
Adhesion	N/C	N/C	-1 unit	N/C	N/C	N/C

N/C: no change

**Figure 12**



**Figure 13A**

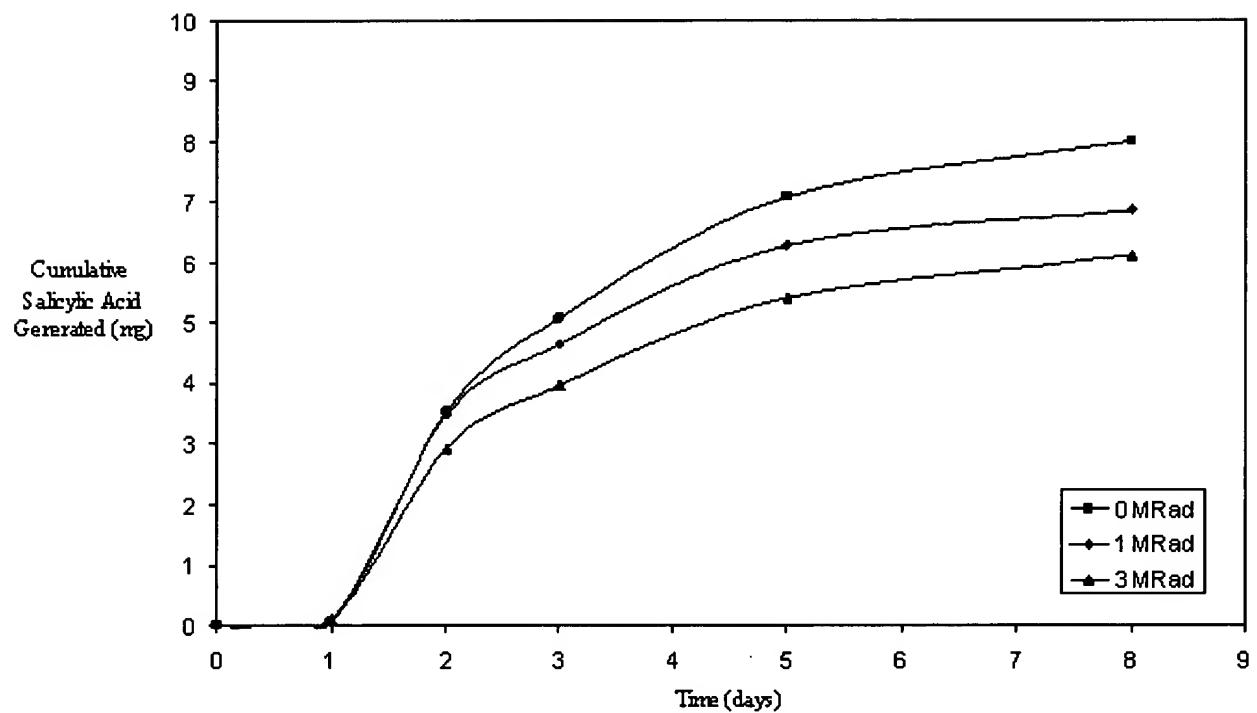


Figure 13B

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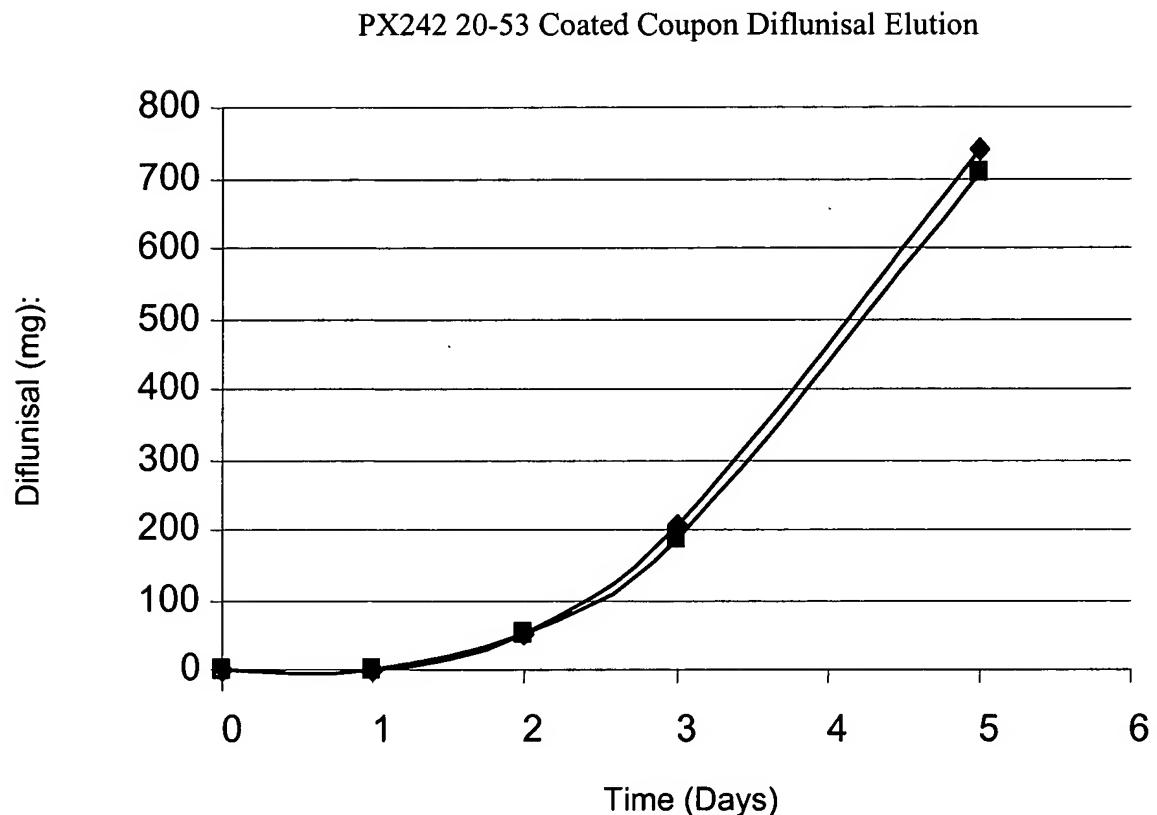


Figure 14

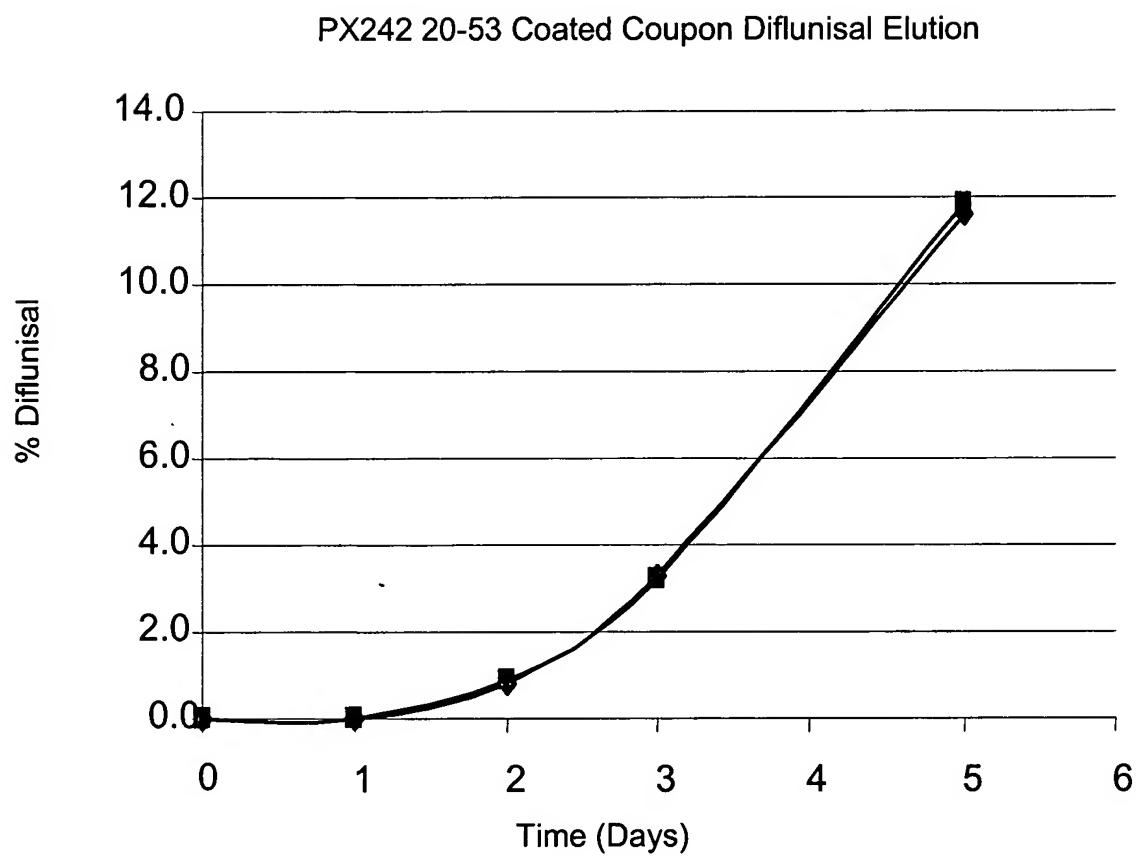
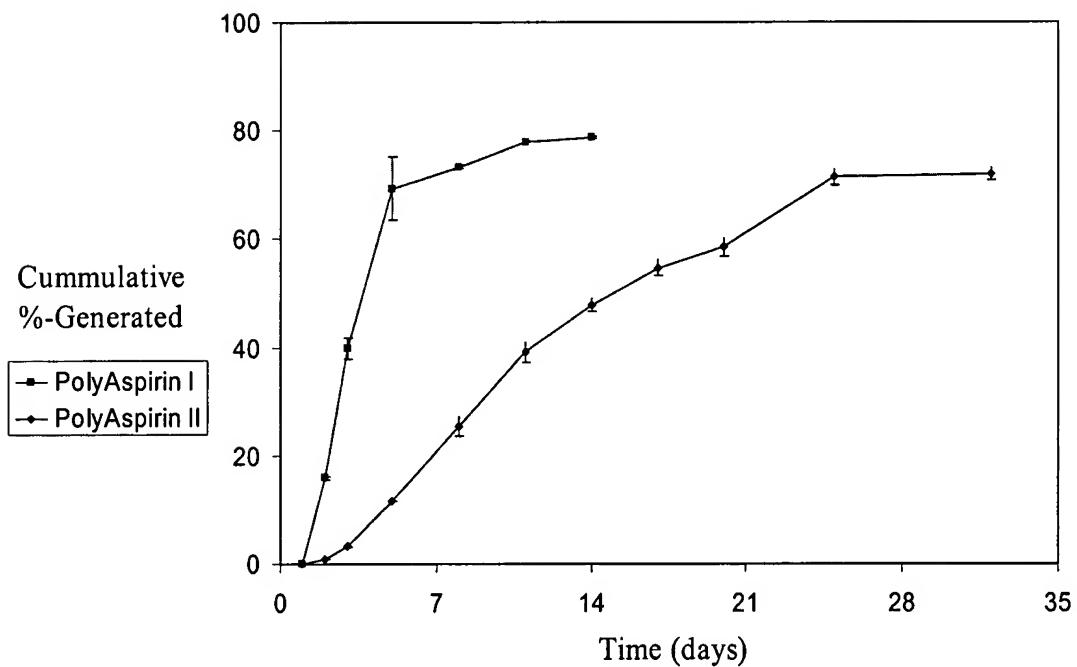


Figure 15

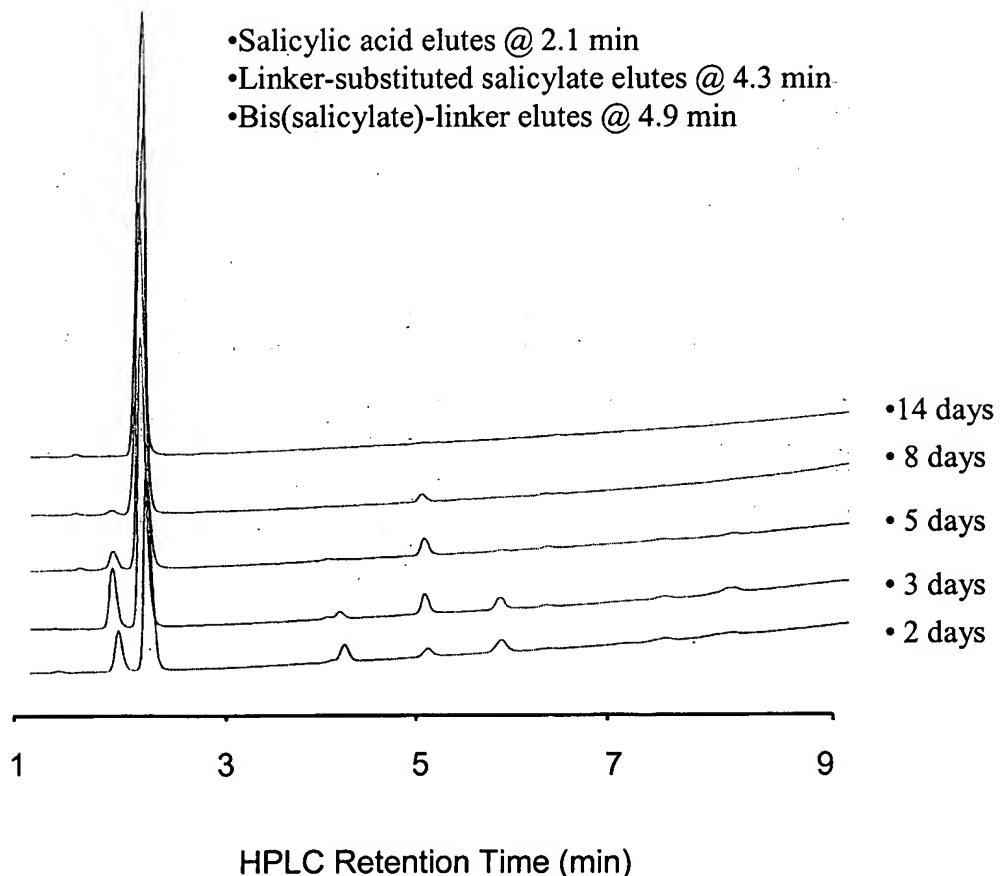
Erosion of PolyAspirin I & II  
Generation of NSAID into 37 °C pH 7.4 PBS from  
~5  $\mu$ m-thick Coatings on 316L SS Plates



**Figure 16**

Erosion Profile for PolyAspirin I

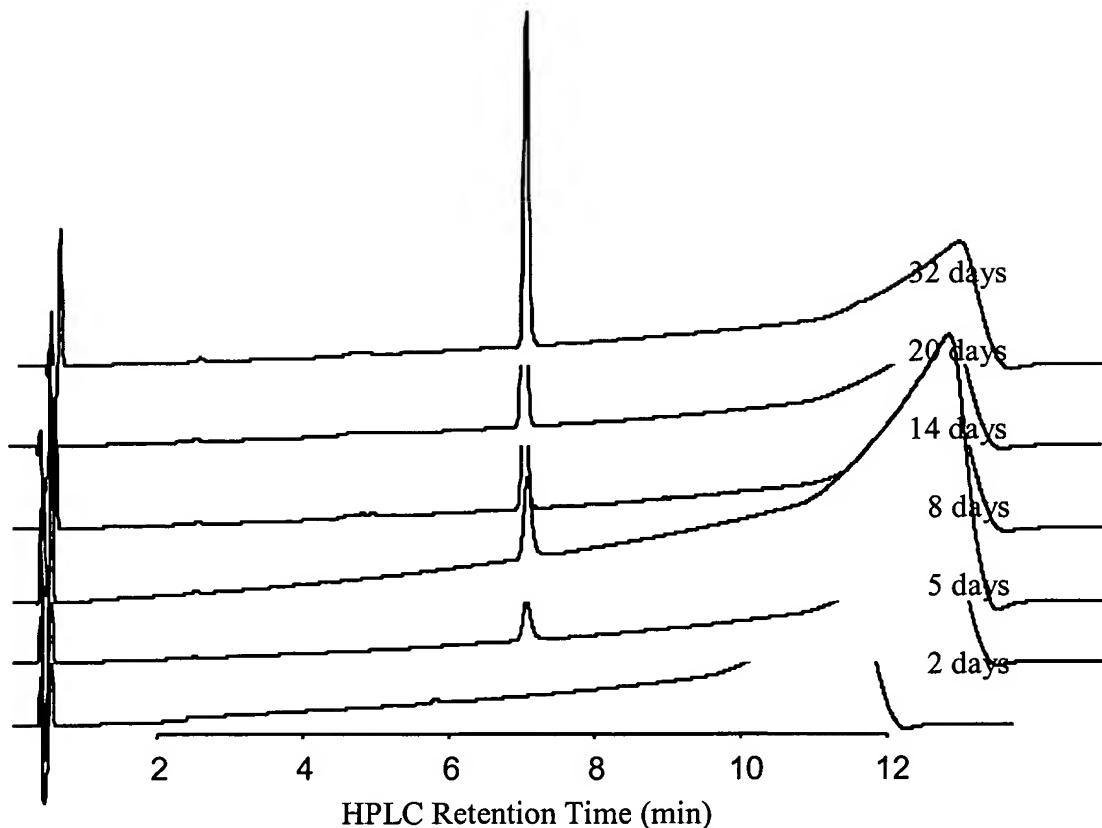
- Salicylic acid elutes @ 2.1 min
- Linker-substituted salicylate elutes @ 4.3 min
- Bis(salicylate)-linker elutes @ 4.9 min



**Figure 17**

Erosion Profile for PolyAspirin II

Diflunisal elutes @ 7.1 min  
Linker-substituted Diflunisal elutes @ 9.0 min  
Bis(diflunisal)-linker elutes @ 12 min



**Figure 18**

Effect of MW on Erosion

Generation of Diflunisal from PolyAspirin II into  
37 °C Serum from Coatings on 316L SS Plates

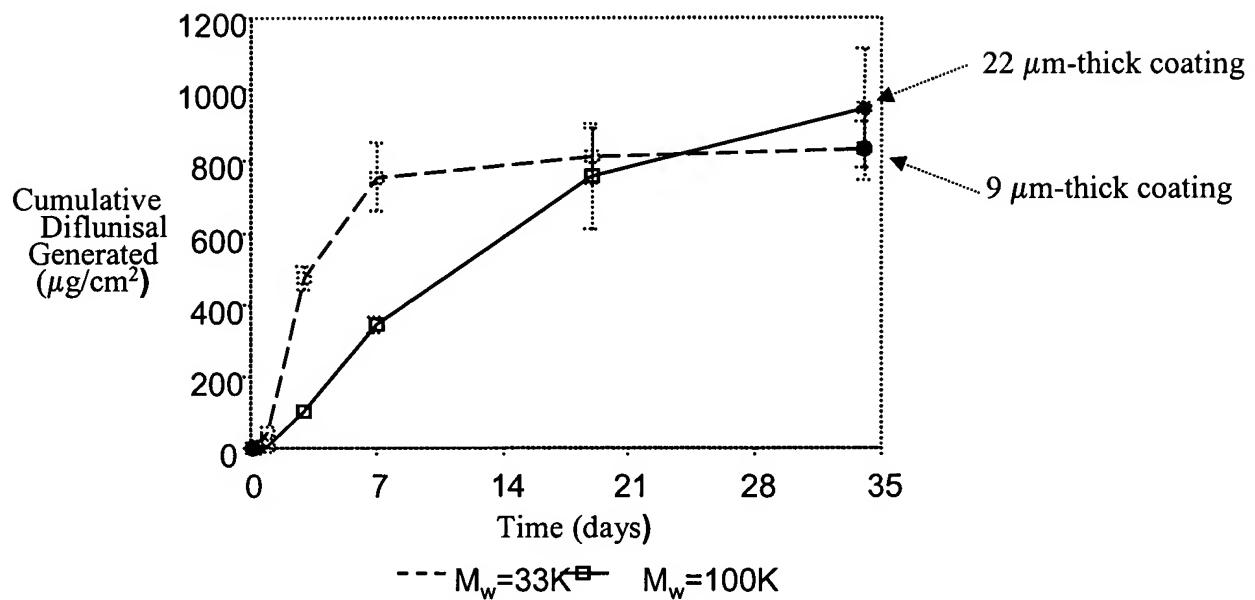
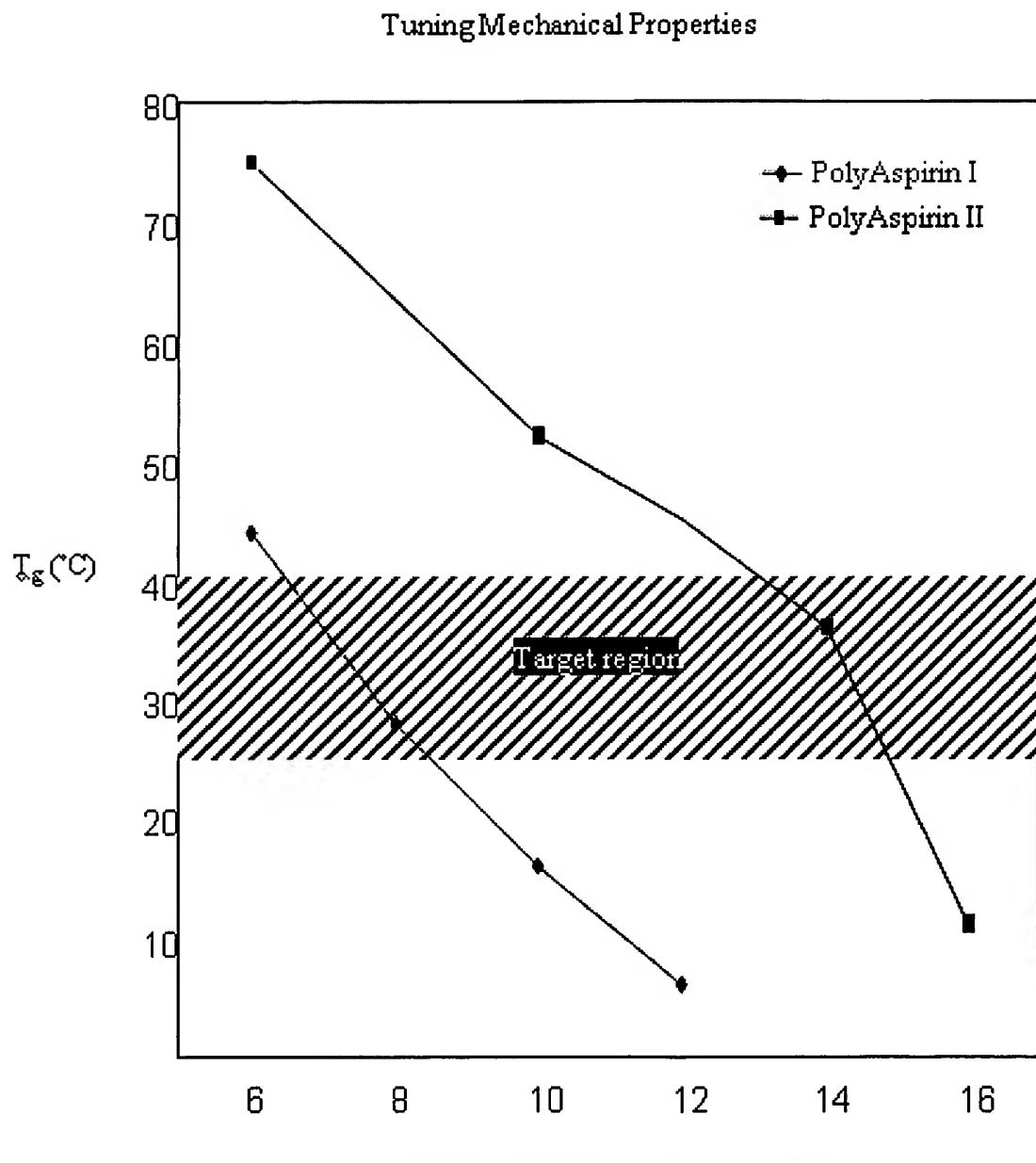


Figure 19



**Figure 20**

Thermoanalysis of PolyAspirin™

Property	PolyAspirin I		PolyAspirin II	
	PX261 Mw ~ 20K		PX657 M <sub>w</sub> ~ 33K	M <sub>w</sub> ~ 100K
T <sub>g</sub> (°C)	29		36	44
Ultimate Stress (kPa)	1700 (25°C) >2000 (37°C)		>2800 (25°C)	>2600 (25°C)
Ultimate Elongation (%)	>500 (25°C) >500 (37°C)		>4 (25°C)	>500 (25°C)
Toughness (kPa)	>3900 (25°C) >4400 (37°C)		>560 (25°C)	>4000 (25°C)

**Figure 21**

Properties of PolyAspirin™ Coatings

Test	PolyAspirin I		PolyAspirin II	
	PX261	Mw ~ 20K	PX657	Mw ~ 100K
<u>Hardness</u>				
Ambient	B		F	3H
5 min in PBS, 37 °C	B		2B	B
1 hr in PBS, 37 °C	-		8B	4B
<u>Flexibility</u>				
Ambient		<3 mm	<3 mm	<3 mm
5 min in PBS, 37 °C		<3 mm	<3 mm	<3 mm
1 hr in PBS, 37 °C		-	<3 mm	<3 mm
<u>Adhesion</u>				
Ambient		5B	5B	5B

Figure 22

PolyAspirin Coatings with Admixtures

Test	PolyAspirin II (PX657)	
	No Admixture	20% Paclitaxel Admixed
<u>Hardness</u>		
Ambient	F	F
5 min in PBS, 37 °C	2B	F
1 hr in PBS, 37 °C	8B	6B
<u>Flexibility</u>		
Ambient	<3 mm	<3 mm
5 min in PBS, 37 °C	<3 mm	<3 mm
1 hr in PBS, 37 °C	<3 mm	<3 mm
<u>Adhesion</u>		
Ambient	5B	5B

**Figure 23**

Erosion of PolyAspirin I & II

Diflunisal Generation & Paclitaxel Release into 37 °C Serum from ~5  $\mu$ m-thick Coatings on 316L SS Plates

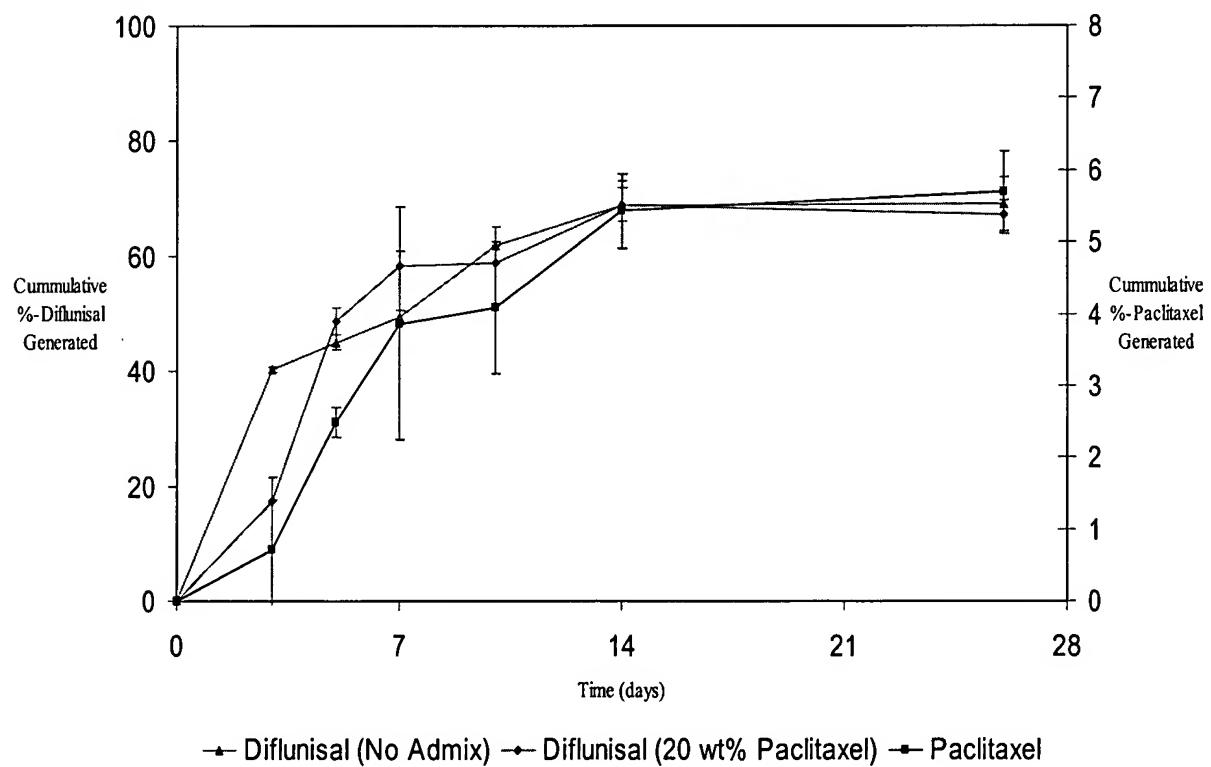
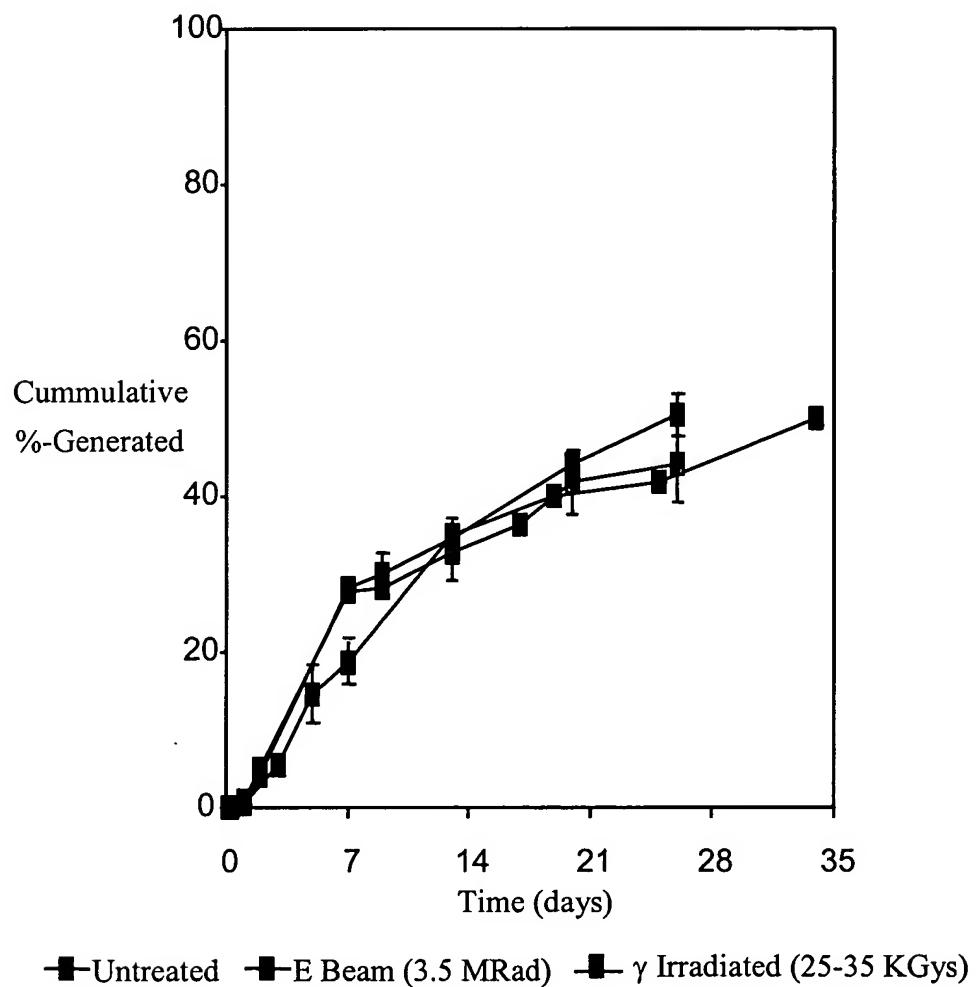


Figure 24

Erosion of Sterilized PolyAspirin II

Generation of Diflunisal into 37 °C Serum from ~5  $\mu$ m-thick Coatings on 316L SS Plates



**Figure 25**

$\gamma$ Irradiation (25-35 Kgy)		
Property	PolyAspirin I	PolyAspirin II
N/C: no change	PX261 $M_w \sim 20K$	PX657 $M_w \sim 100K$
MW	N/C	-50%
Hardness	-2 units	-3 units
Flexibility	N/C	-
Adhesion	N/C	-

**Figure 26**

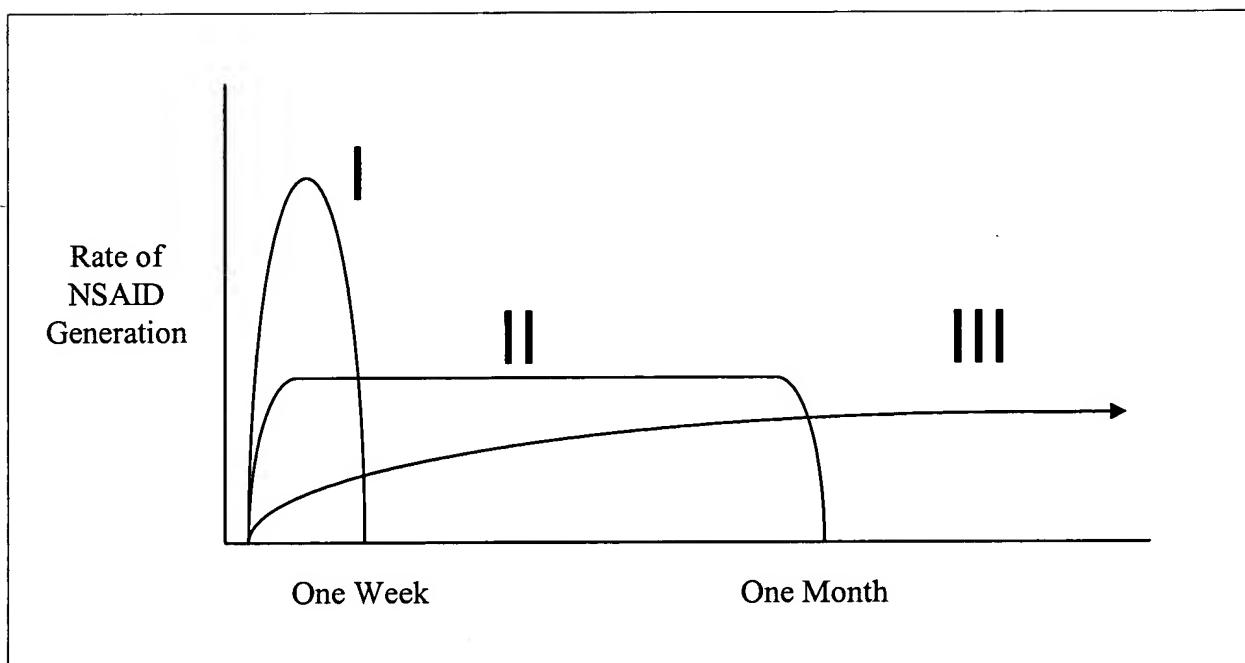
E Beam (3-4.5 MRad)

•Property	•PX261 • $M_w \sim 20$ K	• $M_w \sim 33$ K	• $M_w \sim 80$ K
•MW	•-26%	•+5%	•-30%
•Hardness	•1 unit •PolyAspirin I	•+2 units •PolyAspirin II	•N/C
•Flexibility	•N/C	•PX657	•N/C
•Adhesion	•-1 unit	•-	•-

**Figure 27**

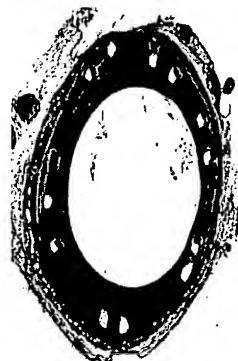
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**Kinetics of NSAID Generation**

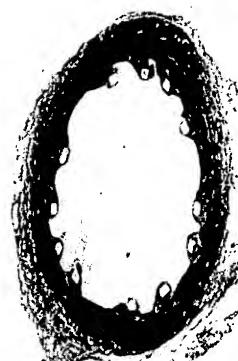


**Figure 28**

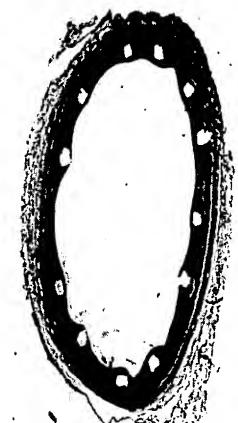
**Figure 29**



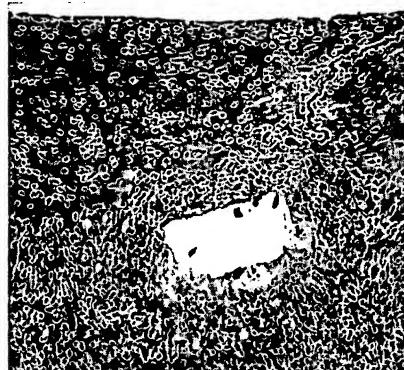
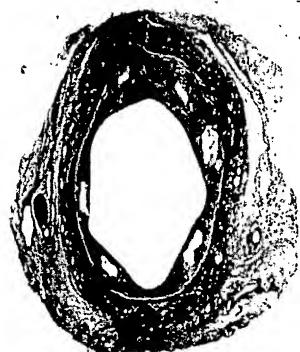
**Figure 30**



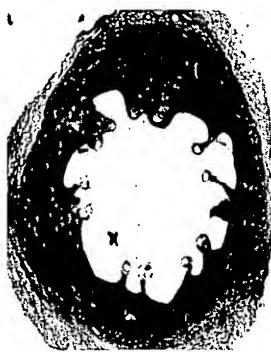
**Figure 31**



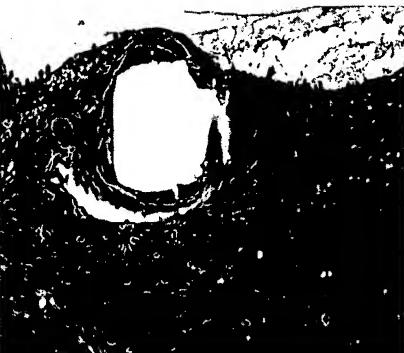
**Figure 32**



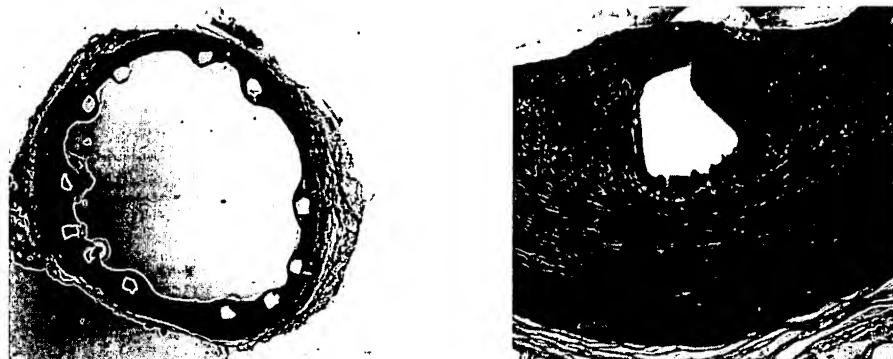
**Figure 33**



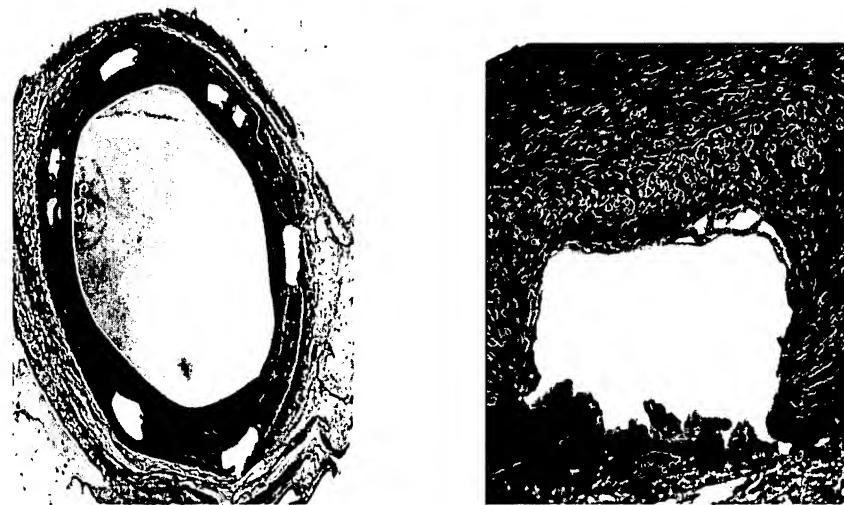
**Figure 34**



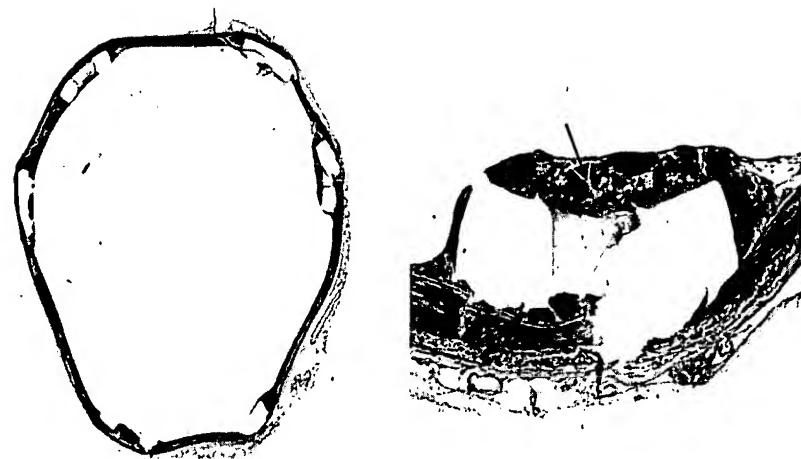
**Figure 35**



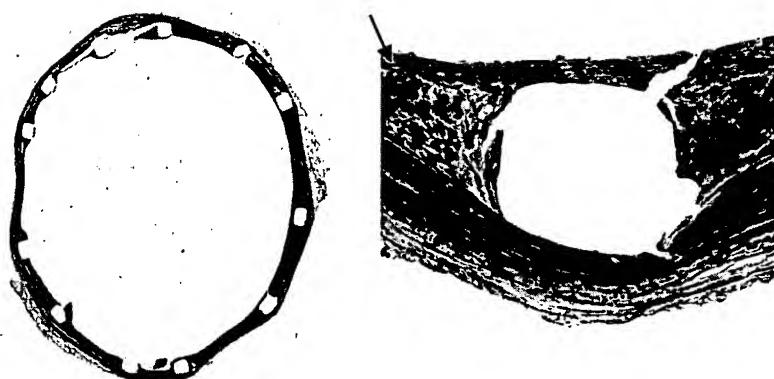
**Figure 36**



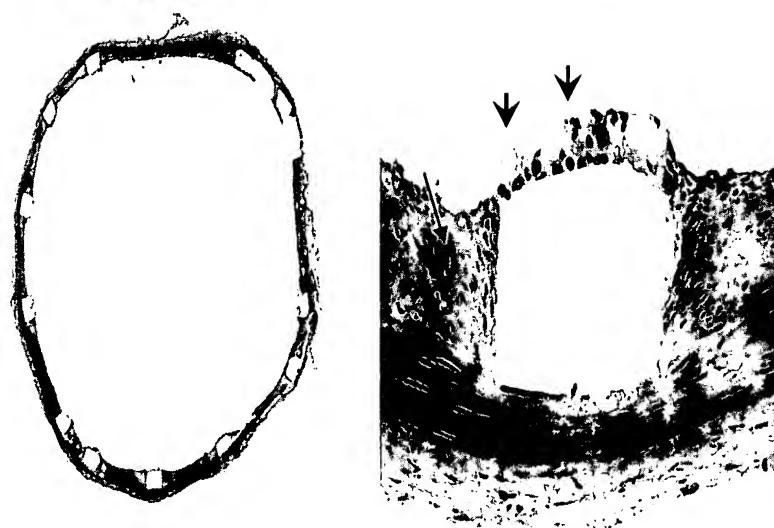
**Figure 37**



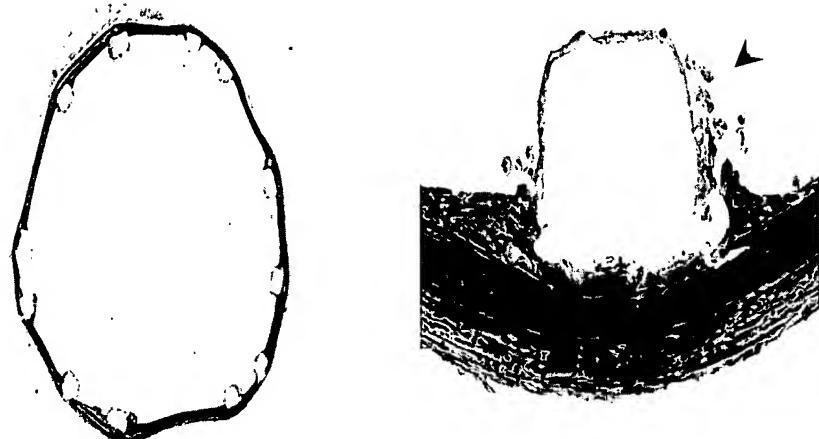
**Figure 38**



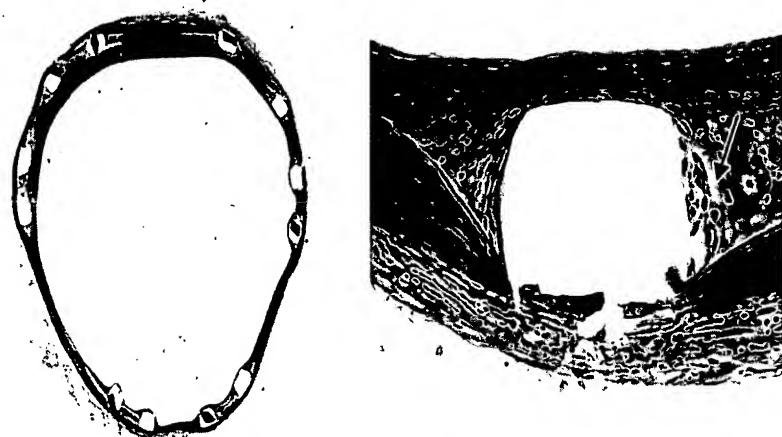
**Figure 39**



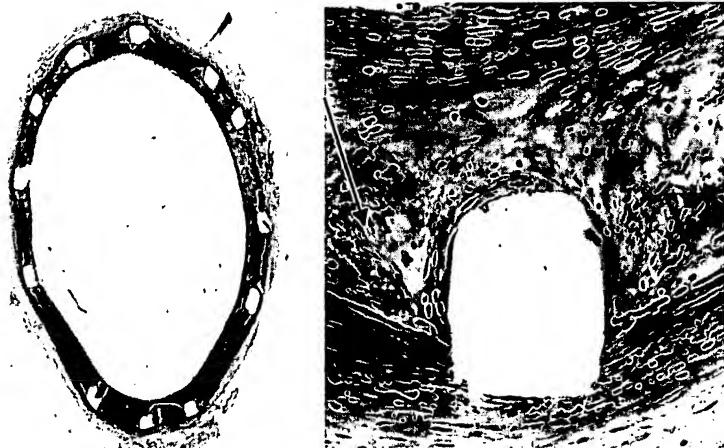
**Figure 40**



**Figure 41**

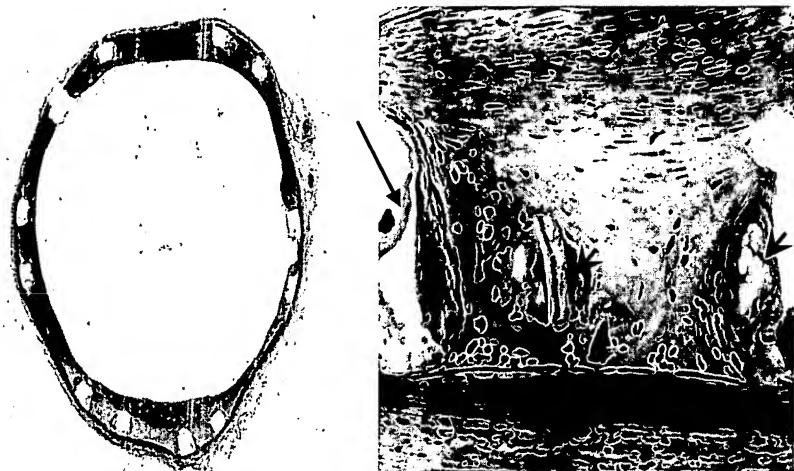


**Figure 42**



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**Figure 43**



uncrimped/unexpanded

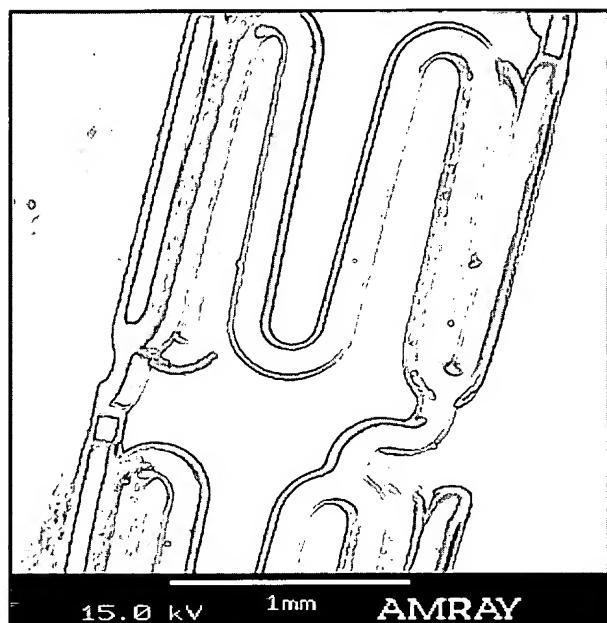


Fig. 44a

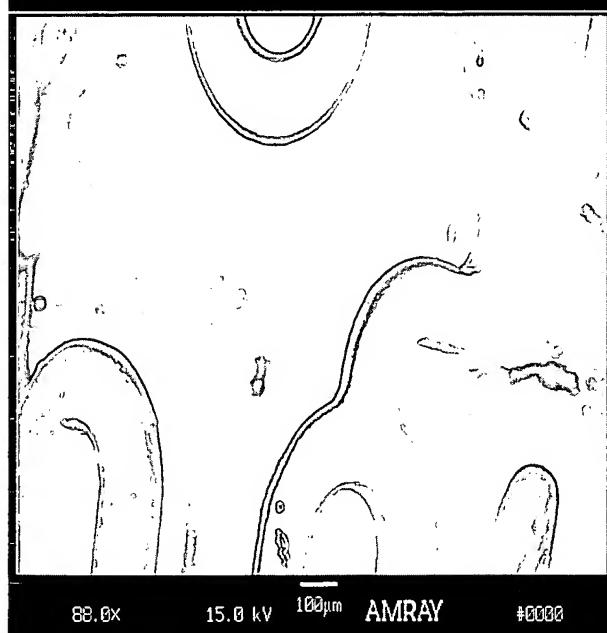
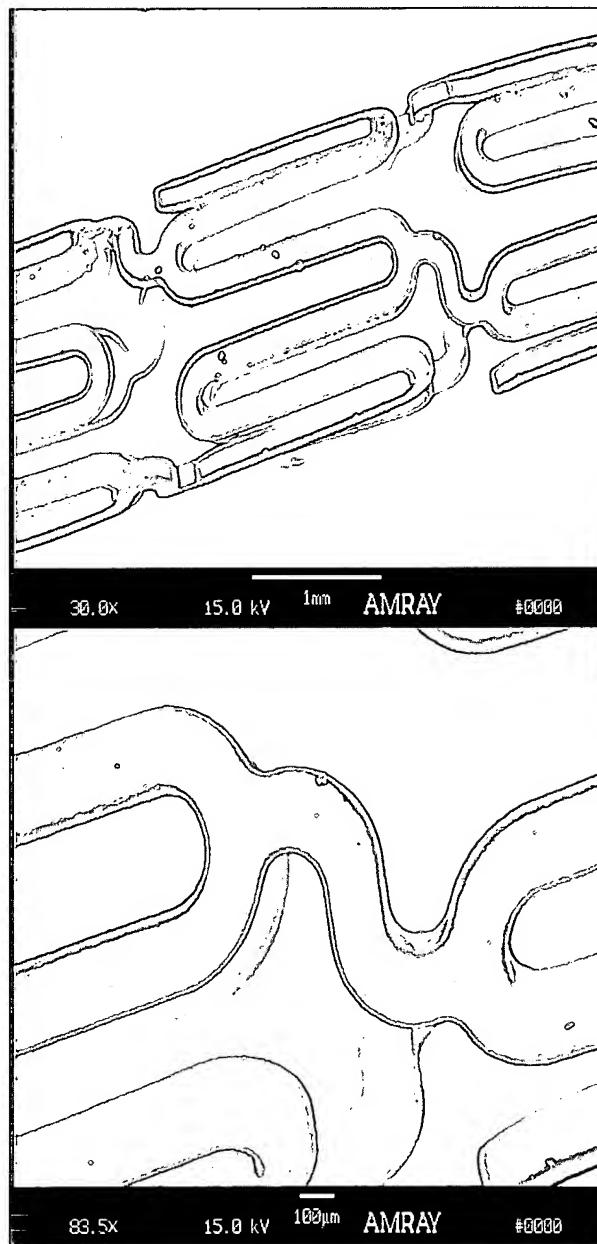


Fig. 44b

**Figure 44**

uncrimped/unexpanded



**Figure 45**

Uncrimped/unexpanded

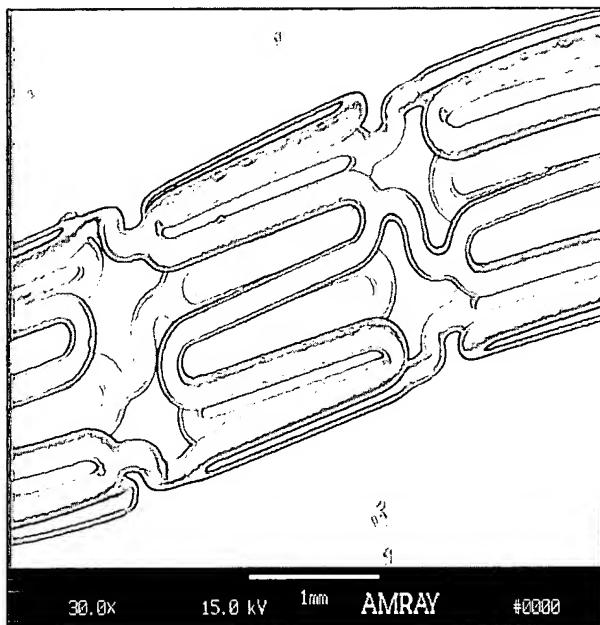


Fig. 46a

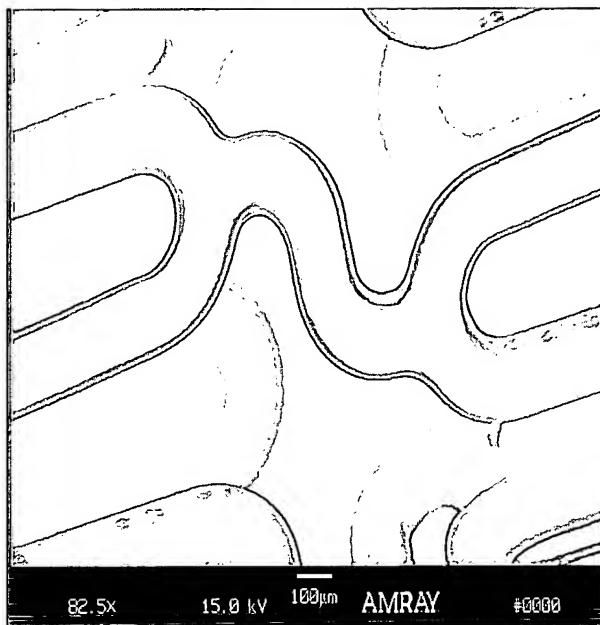
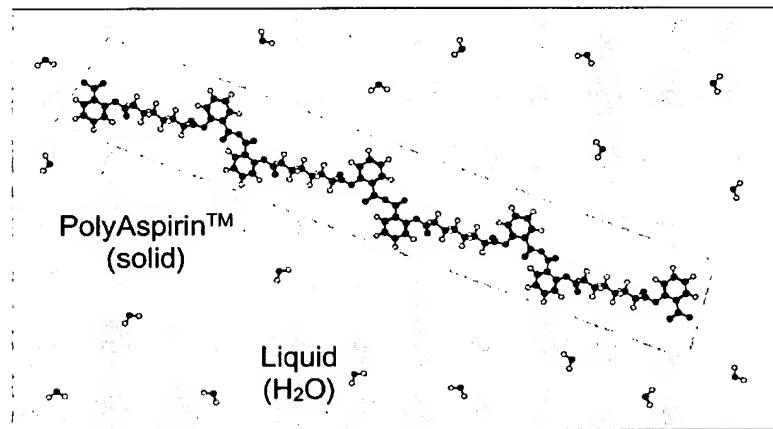


Fig. 46b

Figure 46

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**Figure 47**

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**Figure 48**

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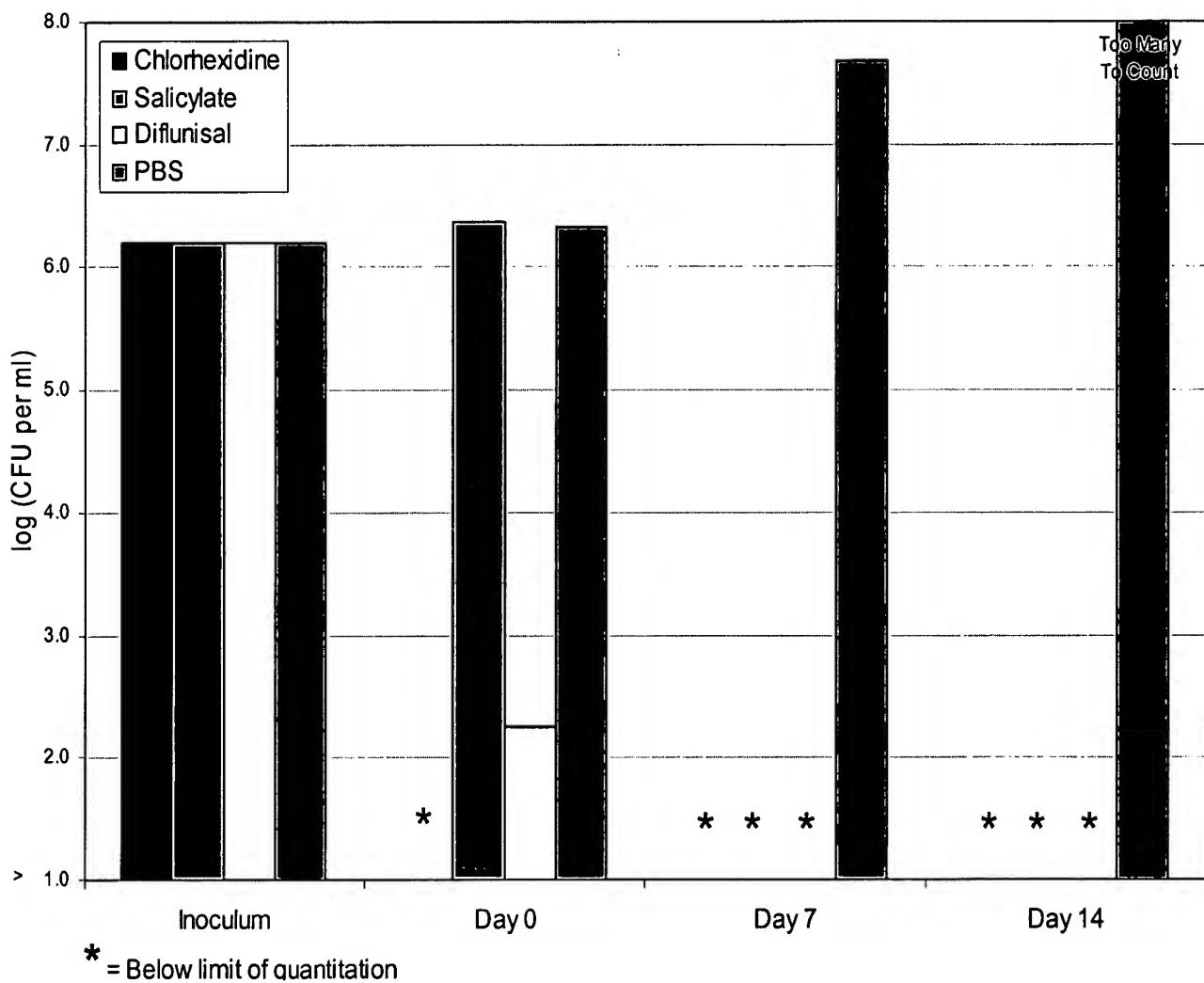


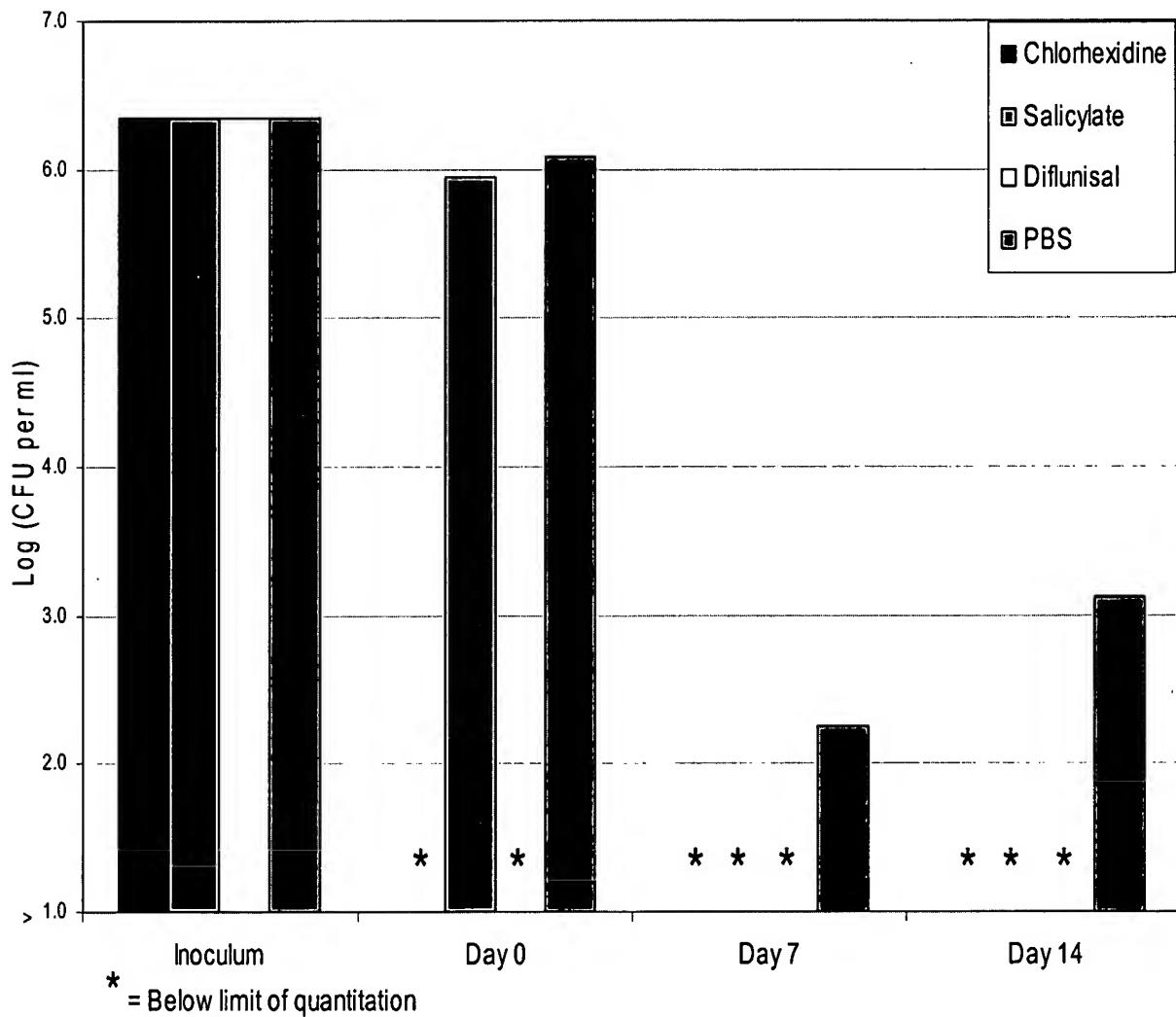
Figure 49

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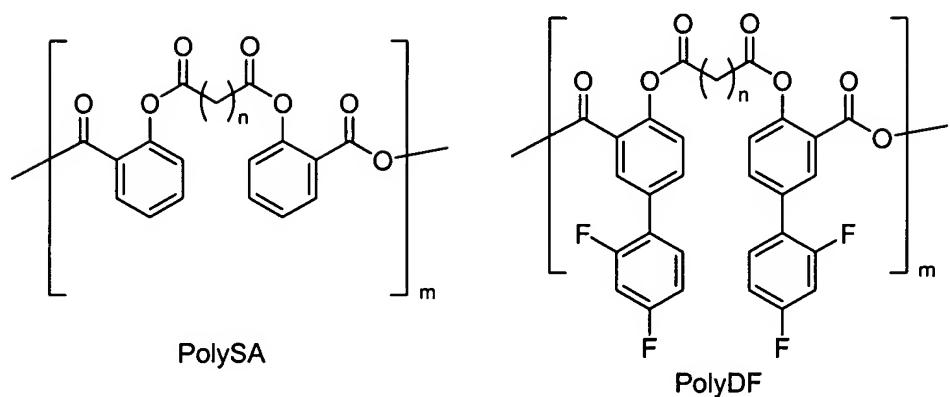
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**Figure 50**

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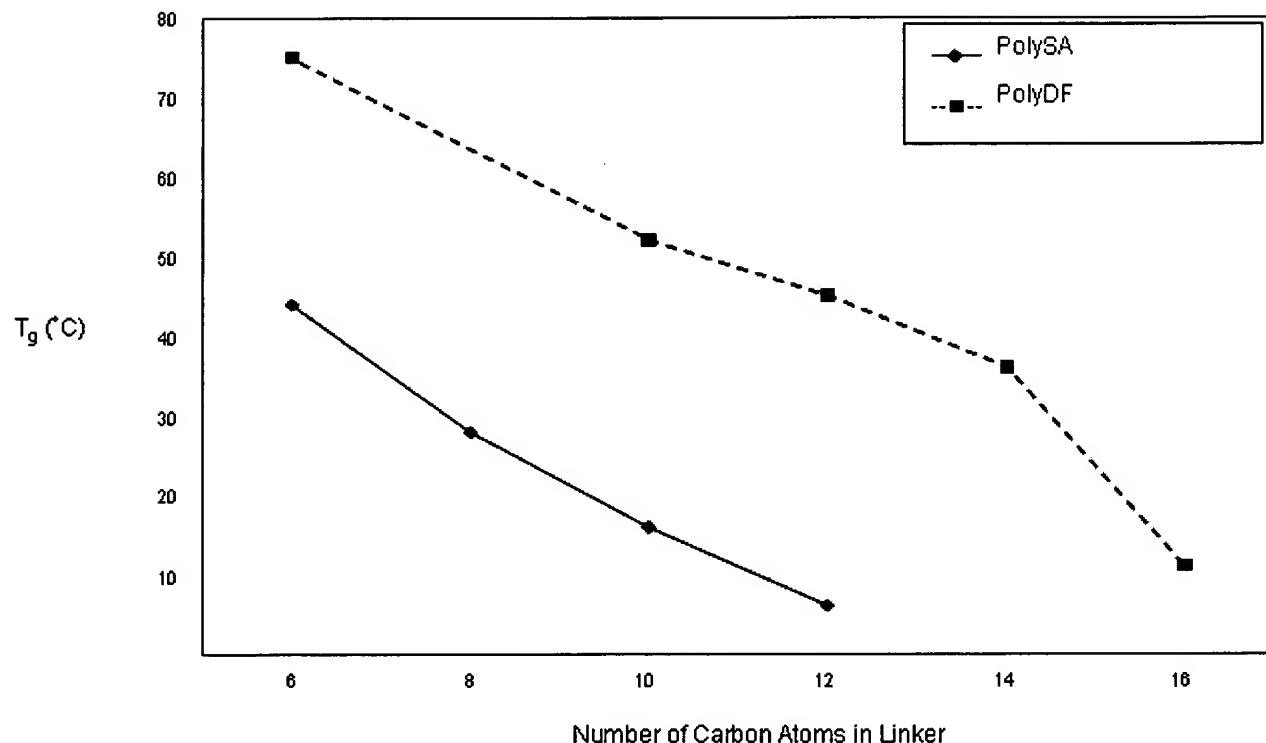
**Figure 51**

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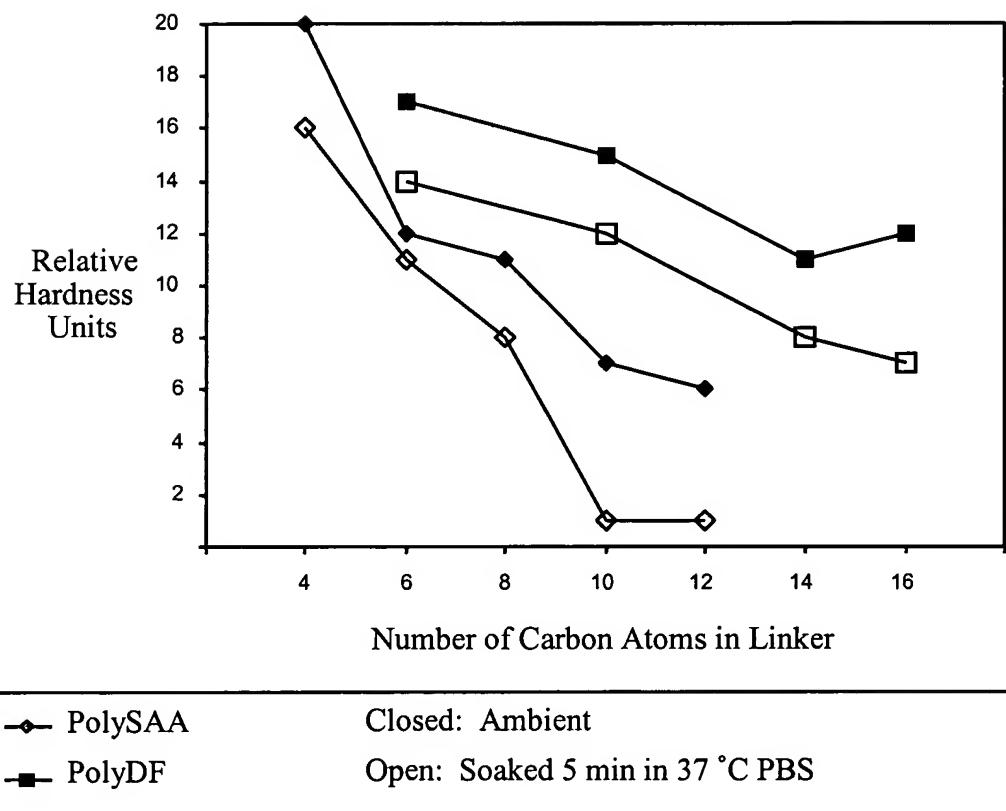
**Figure 52**

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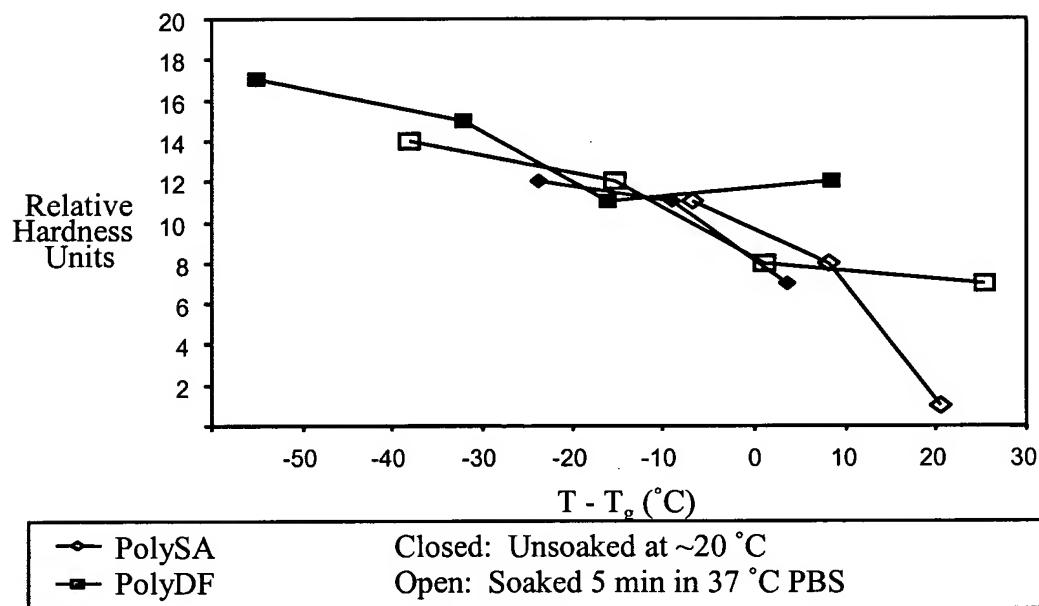
**Figure 53**

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**Figure 54**

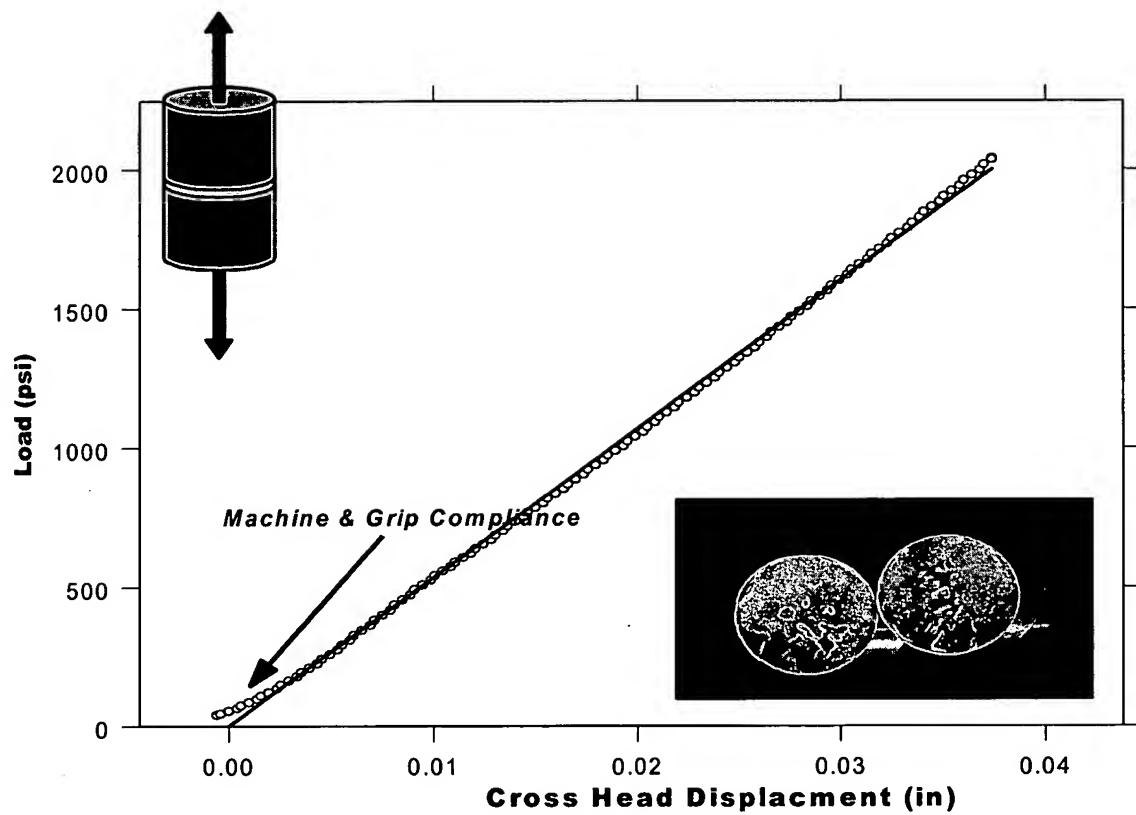


Figure 55

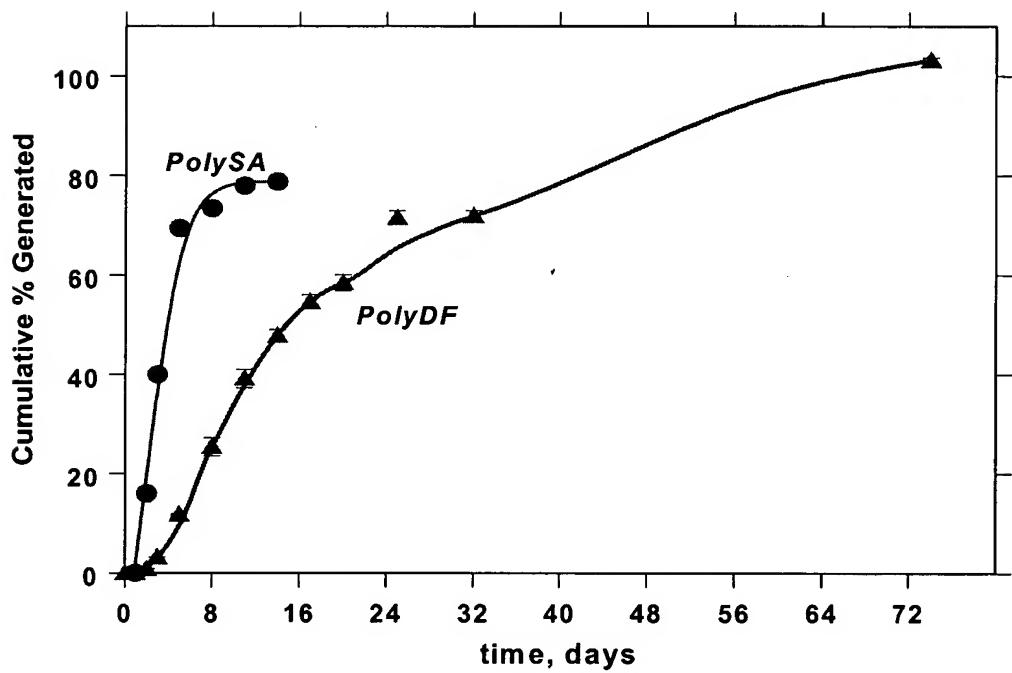
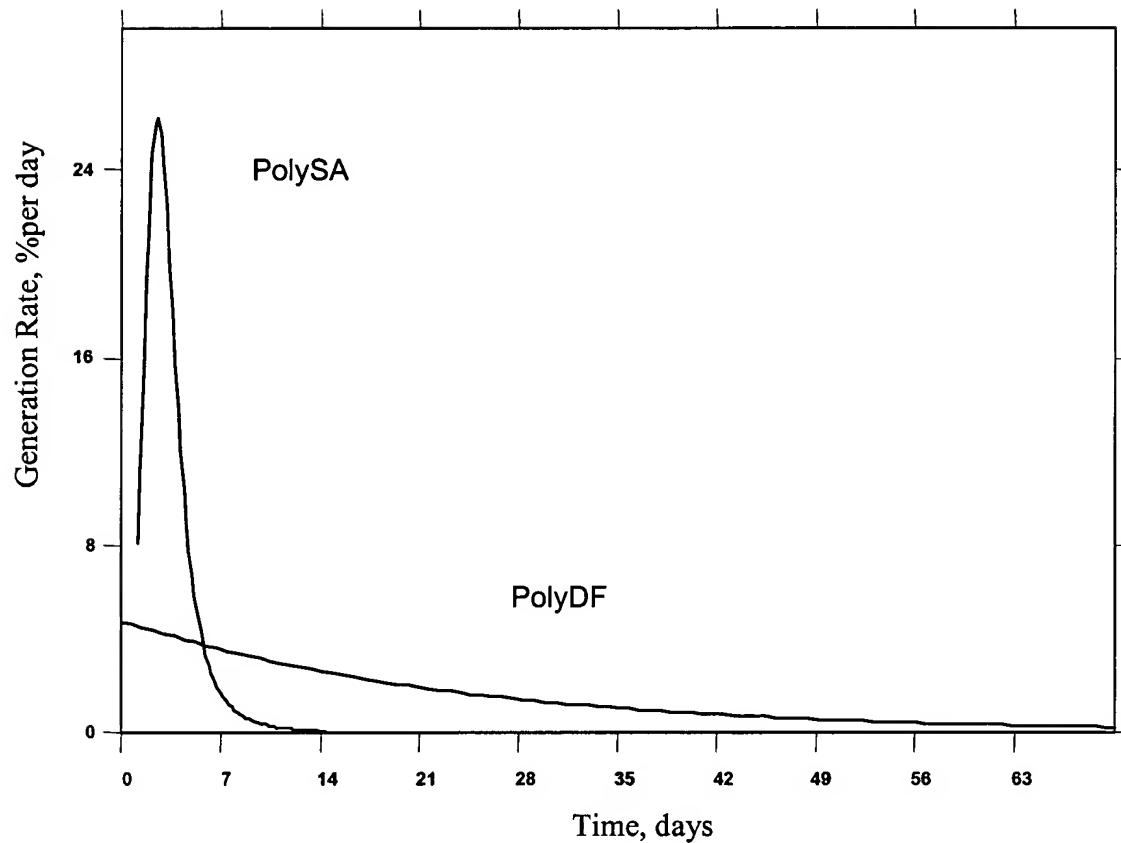


Figure 56



**Figure 57**

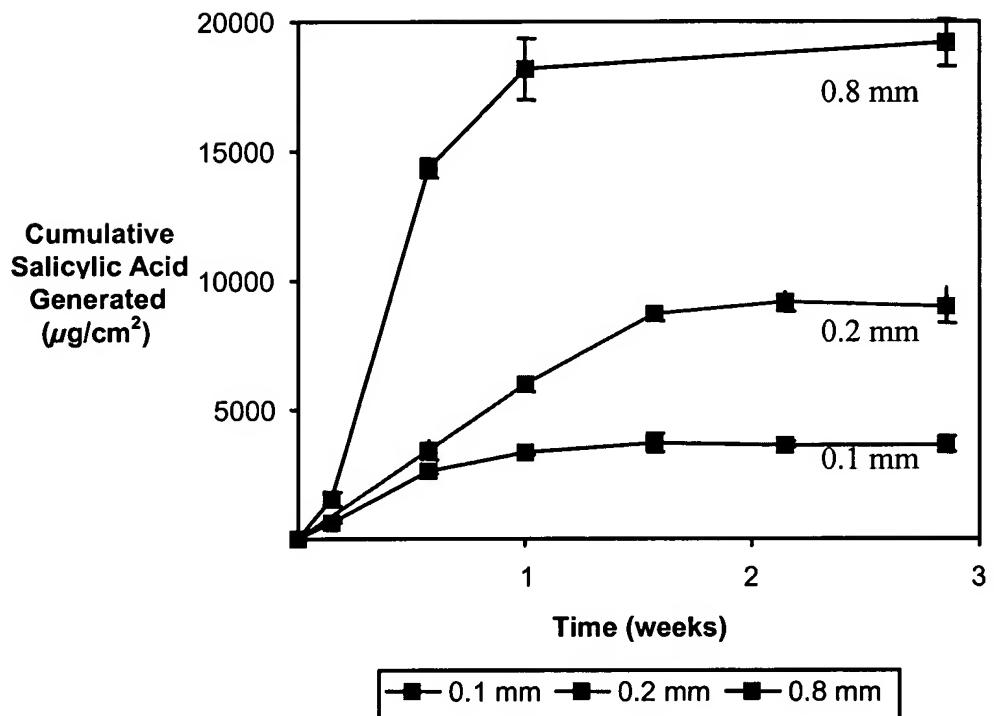


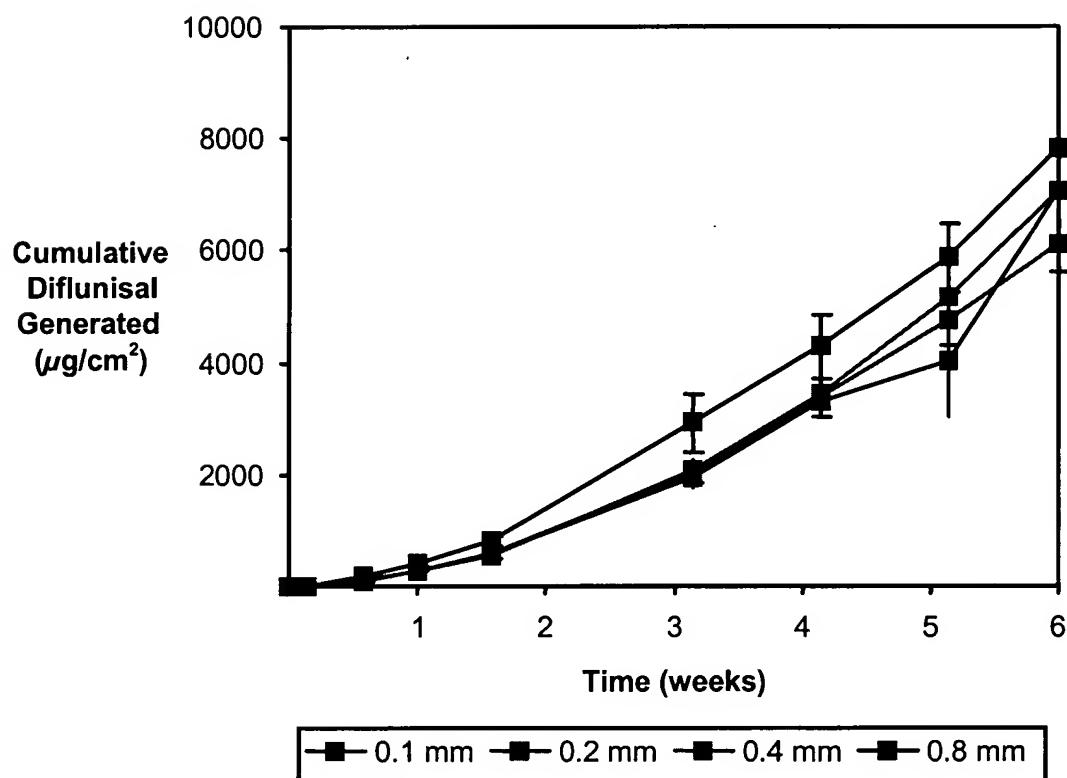
Figure 58

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**Figure 59**

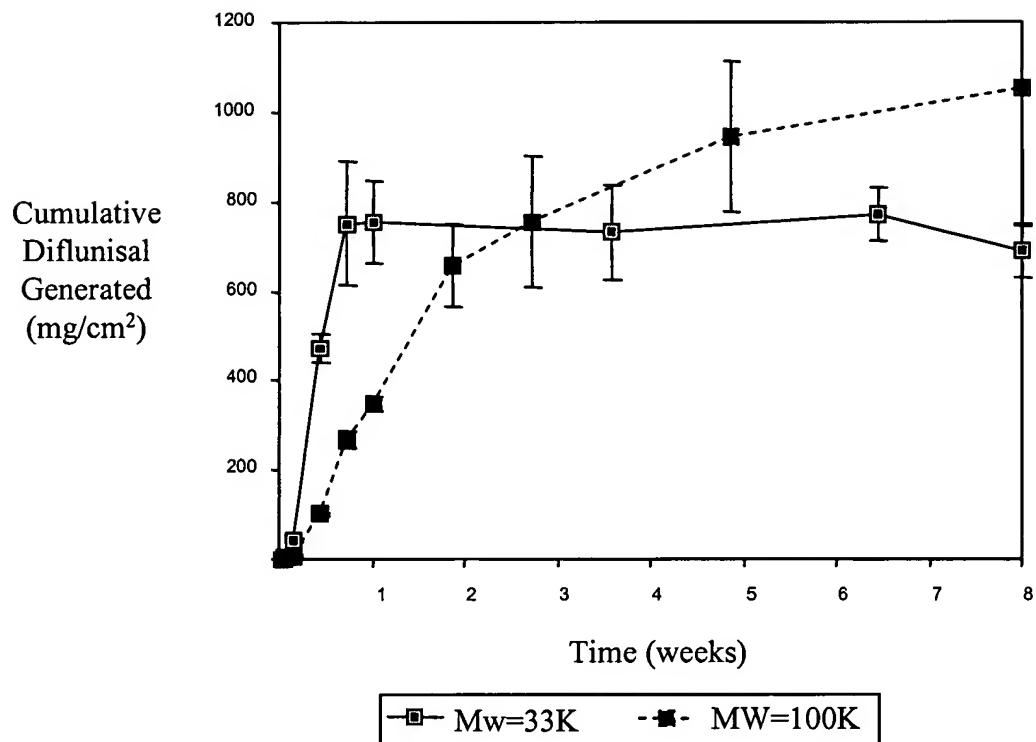


Figure 60

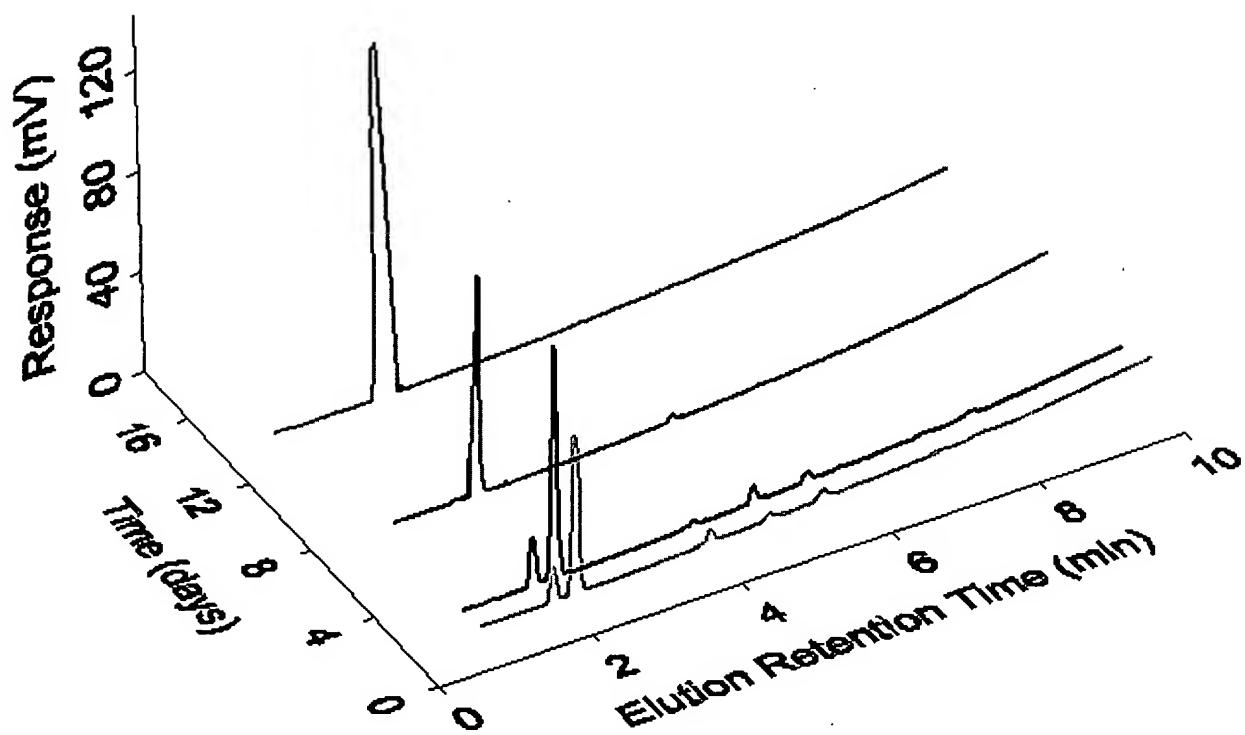
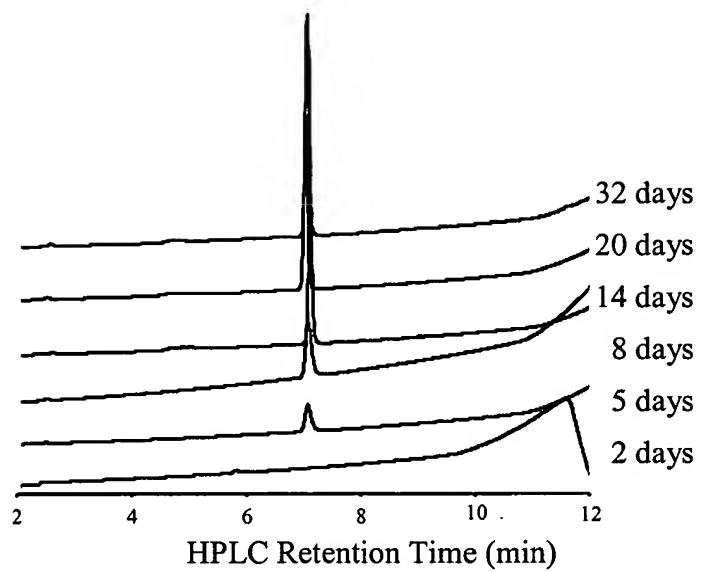
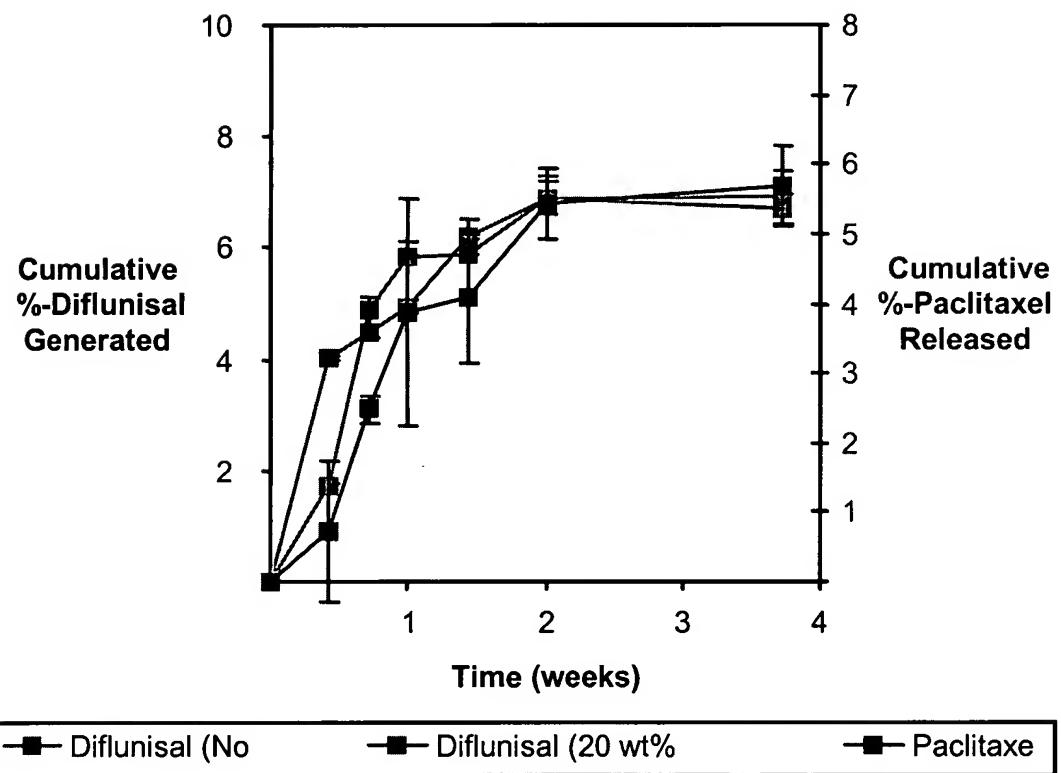


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**Figure 62**



**Figure 63**

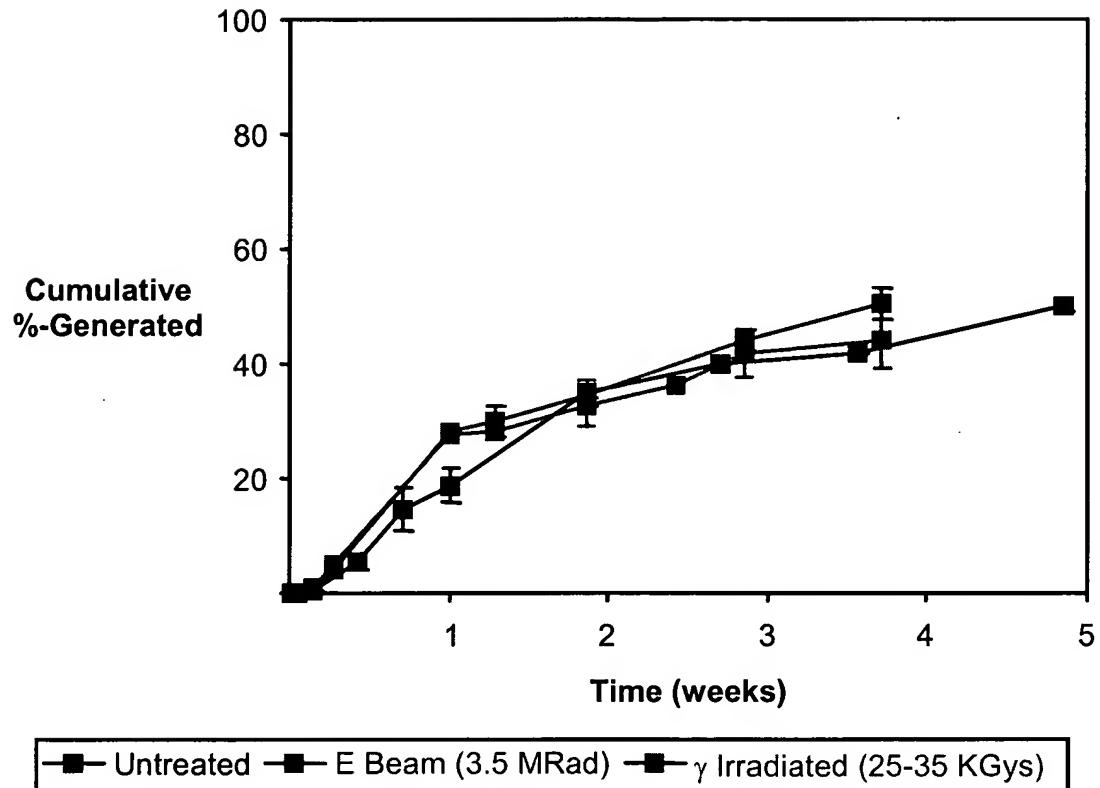
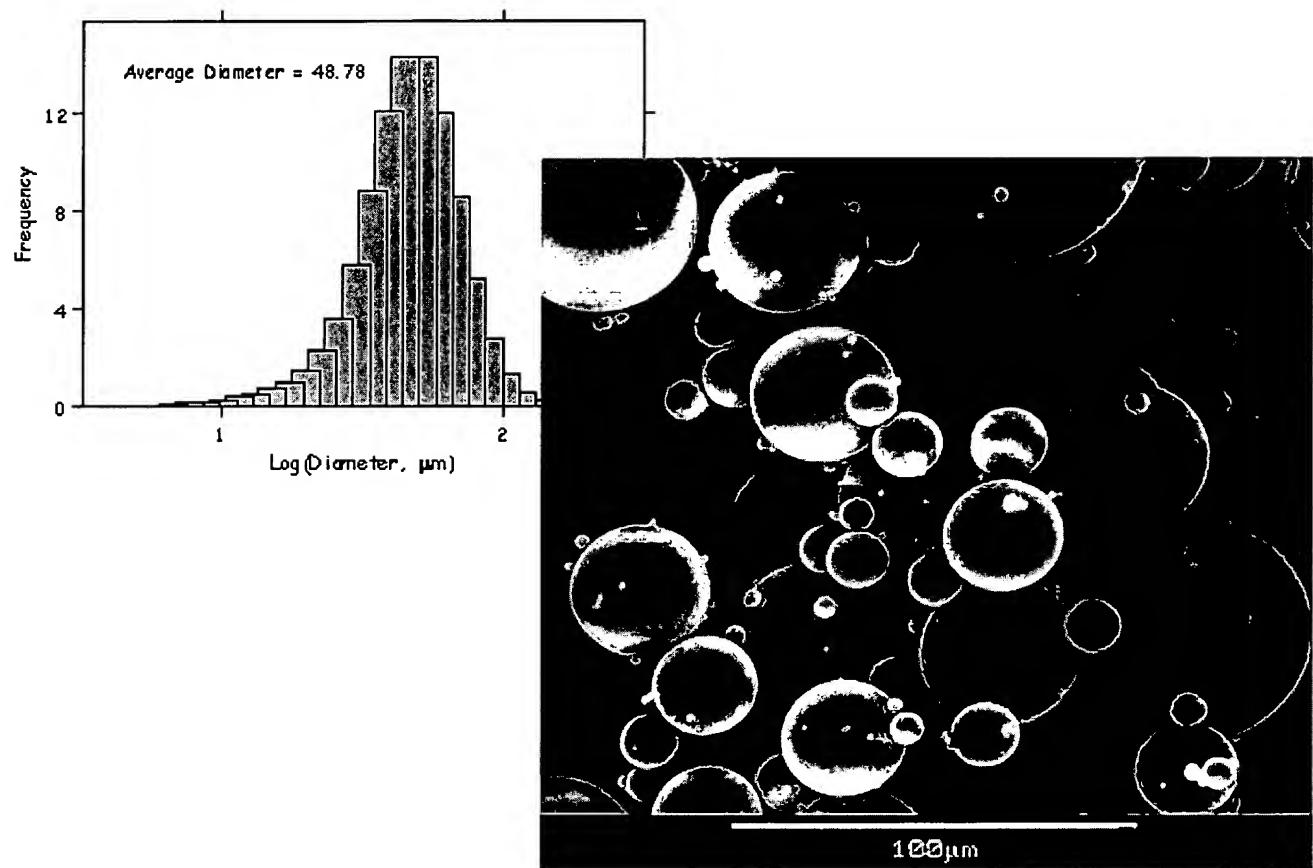


Figure 64



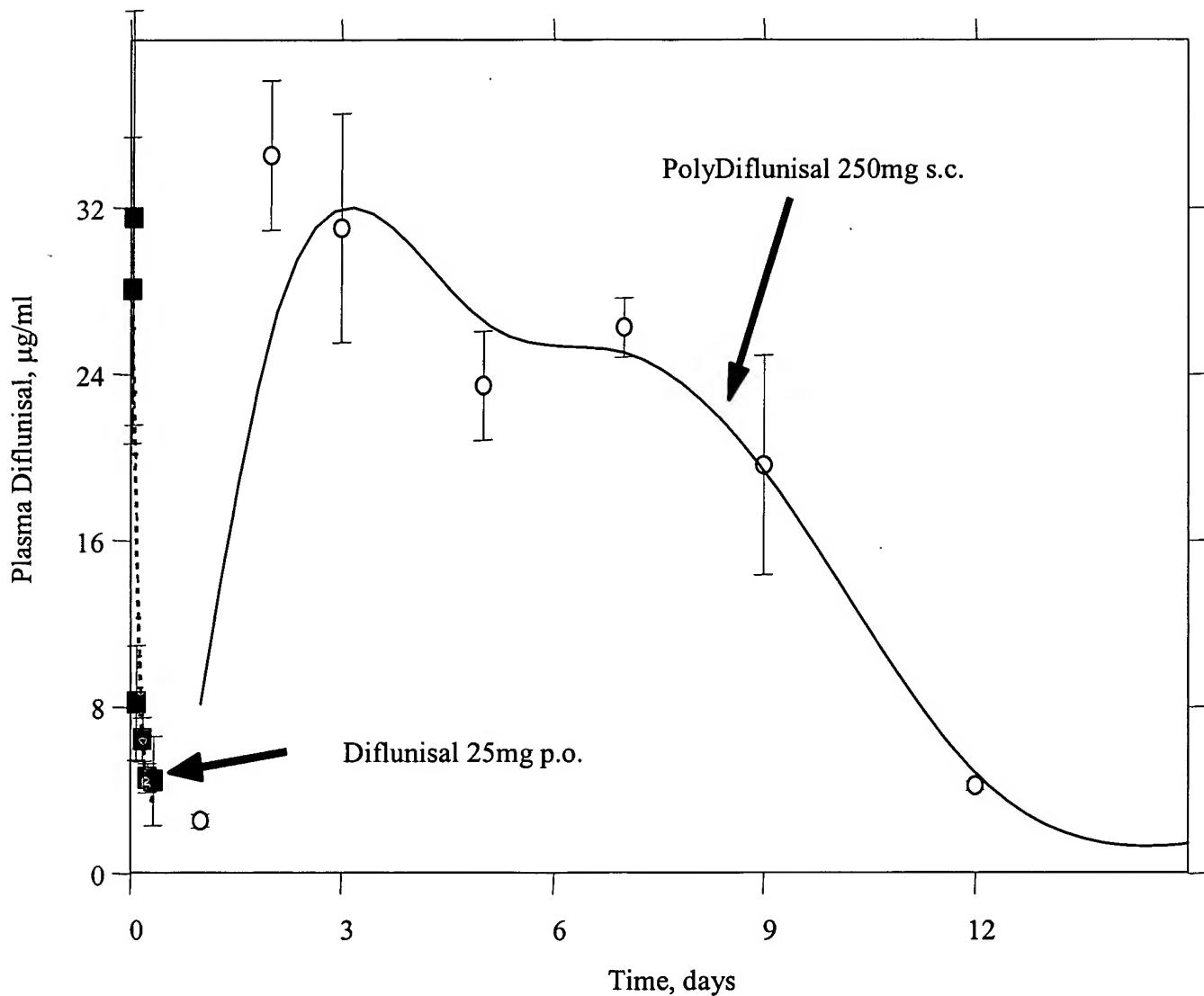
**Figure 65**

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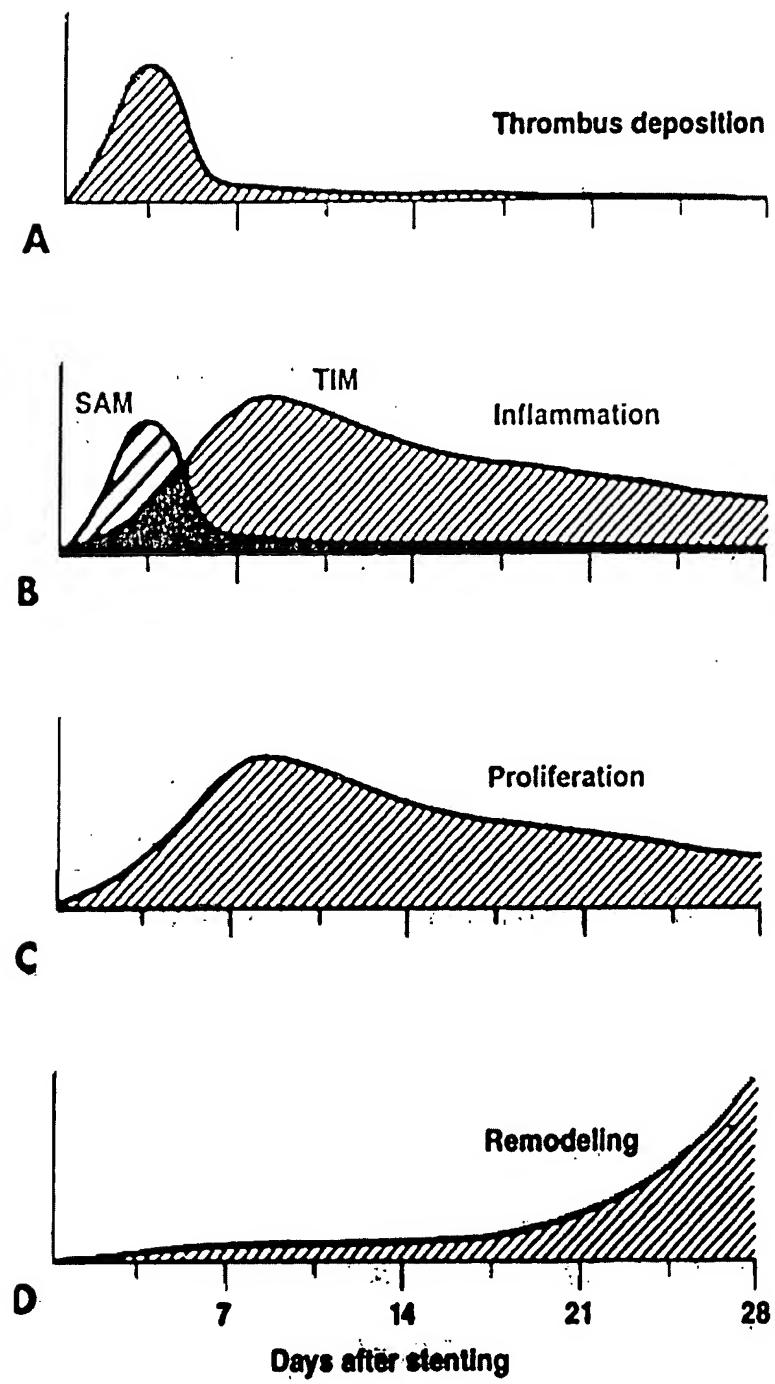
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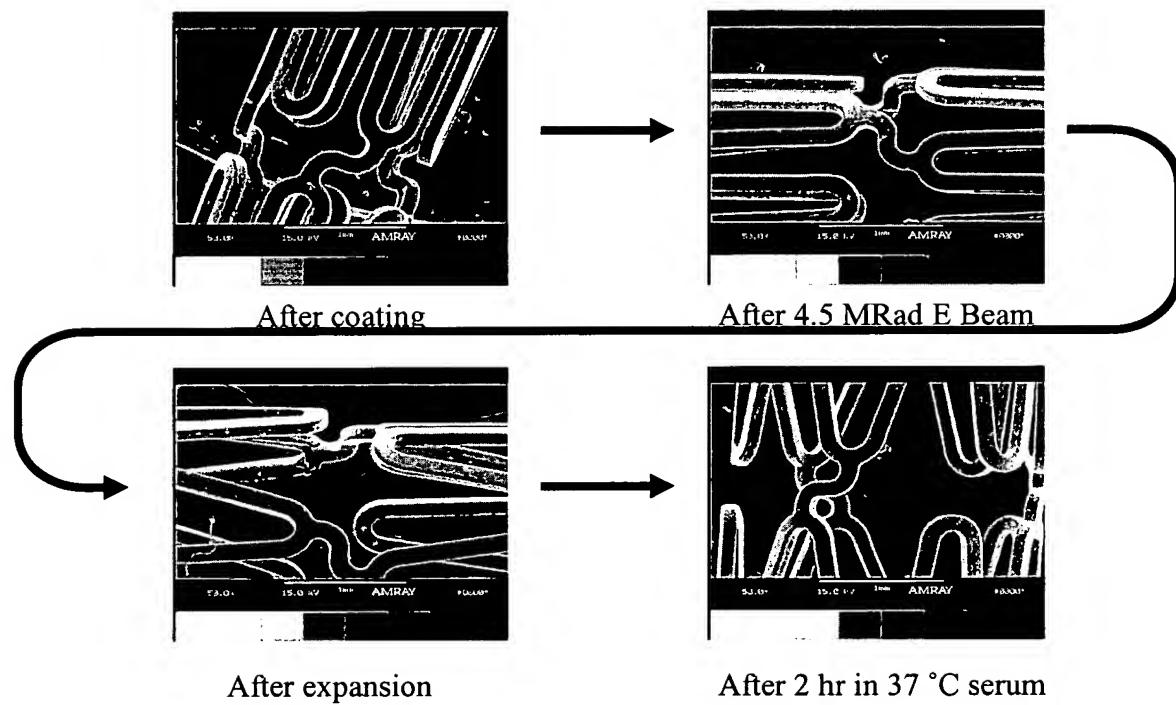
Sheet 59 of 63



**Figure 66**



**Figure 67**



**Figure 68**

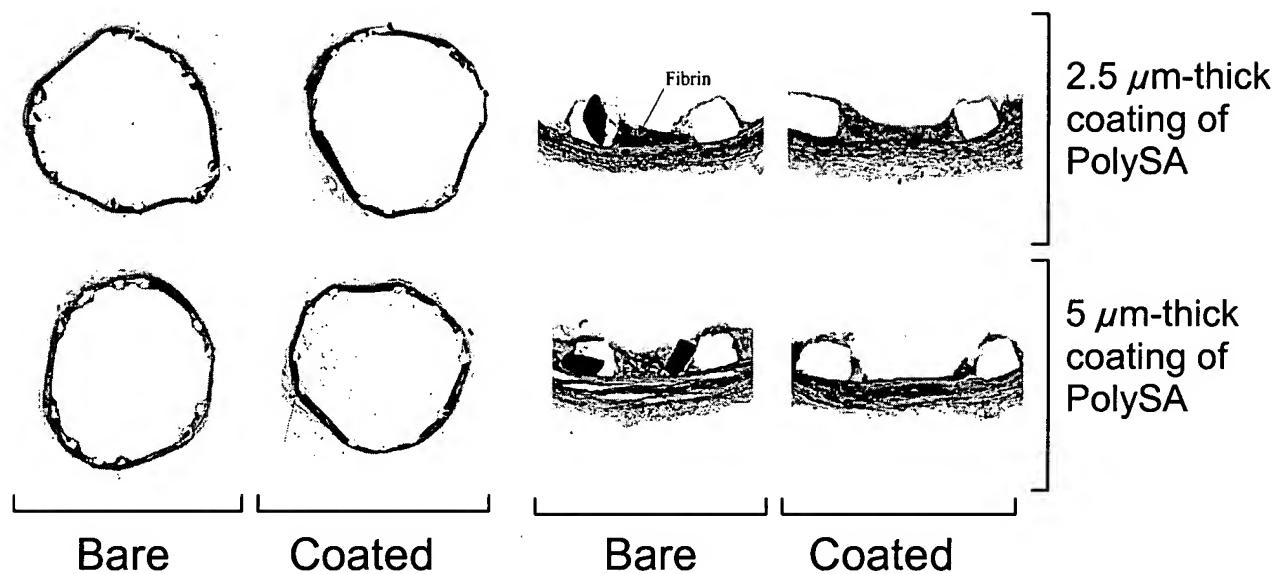
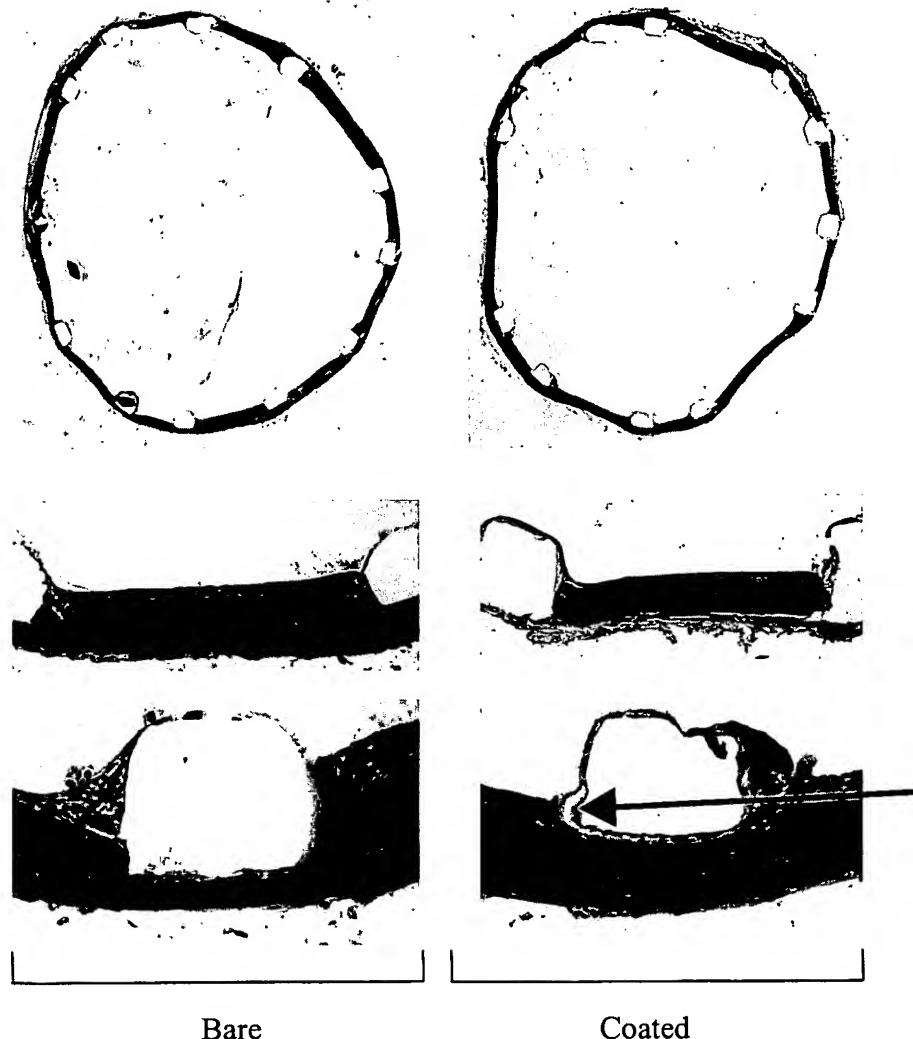


Figure 69



**Figure 70**

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